METACOGNITION AND INSIGHT IN HEALTH, PSYCHOSIS AND DEMENTIA: RELATIONSHIP WITH MOOD AND NEUROCOGNITION

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METACOGNITION AND INSIGHT IN HEALTH, PSYCHOSIS AND DEMENTIA: RELATIONSHIP WITH MOOD AND NEUROCOGNITION

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DECLARATION

I, Emma Claire Palmer, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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STATEMENT OF CONTRIBUTION

This document was written as a doctoral thesis by Emma Palmer. Sections of this thesis have been altered and used in publications, where collaborators have also been involved.

The meta-analysis in Chapter 6 has been submitted for publication. The student carried out the literature search, data entry, data analysis and discussion. The introduction of this publication was based on Chapter 3.2 of this thesis where collaborators made comments. Comments were made after the writing of this thesis and therefore were not incorporated.

Some of the results reported in chapter 7 were published in 2014, along with an introduction that was formed from parts of chapter 2.3 where collaborators made contributions. Amendments to the introduction made by collaborators were not incorporated into this thesis.

Supervisors and collaborators gave advice regarding methods used in this thesis and the student completed analysis of data. Guidance was given on the introductory and discussion chapters by supervisors but the student completed all writing.

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ABSTRACT

Lack of awareness of illness (insight) is a well recognised problem in clinical syndromes such as first episode psychosis and dementia. In healthy persons, ability to accurately rate our thoughts and behaviours is also often referred to as metacognition and there is also some debate as to whether the accuracy of our self-awareness diminishes during healthy ageing. Low mood is often noted to be associated with better insight in clinical groups, however it is not clear whether this also mediates awareness is healthy adults. Some aspects of insight are also mediated by cognitive abilities; more work is required in this area in healthy adults.

Awareness and metacognition are often used interchangeably in the clinical literature, despite the methods differing drastically between healthy and clinical awareness studies.

The aims of this thesis were:

- to investigate the similarities and differences between insight and experimental measures of metacognitive efficiency across the adult life span and in patients experiencing their first episode of psychosis (FEP), early-stage dementia (ED) and depression.
- to quantify the insight and metacognitive functional abilities and deficits in these groups.
- to investigate the effect of mood and cognitive abilities on insight and metacognitive efficiency.
- to run a pilot neuroimaging study aimed at investigating the structural neural correlates of both cognitive insight and metacognitive efficiency in ED patients.

Both clinical measures of insight and experimentally derived metacognitive tasks were used.

Results indicate age, memory and mood mediate metacognitive efficiency in healthy adults, with small associations between metacognitive efficiency and some measures of insight when controlling for age.

In patients, results suggest that mood is associated with cognitive insight in FEP, but not metacognitive efficiency in either early dementia or psychosis. Further, there was an association between cognition and metacognitive efficiency in FEP, but not ED. There was no association between insight and metacognitive efficiency in either patient group.

Comparing groups, FEP patients have worse metacognitive efficiency that healthy younger adults but not insight, whereas there was no difference between ED and healthy older adults. FEP patients appear to have better self-reflection on clinical scales than ED patients, whereas there was no difference between the two groups in metacognitive efficiency.

The imaging study indicated that measures of cognitive insight and metacognitive efficiency have overlapping structural correlates in the cortical midline structures.

Implications for these findings in both healthy adults and patients are discussed.

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OVERVIEW

This thesis comprises a number of studies designed to explore the cognitive and neural systems underlying a number of self-awareness concepts: metacognitive efficiency (the efficiency with which one evaluates one's cognitive performance) and clinical measures of insight (awareness that one is ill). The studies involved 20 patients with first episode psychosis (FEP) and 18 with early-stage dementia (ED), who often have problems with awareness of their illness, as well as 73 healthy adults and 15 patients with self-reported symptoms of depression and scores higher than 15 on Beck Depression Inventory.

The aims included: clarifying the similarities and differences between the broader constructs of clinical insight and the more experimental measures of metacognitive efficiency, in all groups. Next, the aim was to quantify the extent of abilities and deficits in these functions in patient samples and their pattern in healthy adults across the life span. A further aim was to investigate how mood and cognition affect insight and metacognitive efficiency, and if this is uniform across the study groups. Finally, a pilot neuroimaging study aimed to investigate the structural correlates of both cognitive insight and metacognitive efficiency in ED patients.

Measures of interest were 1) cognitive insight, which is a concept comprised of two sub-components; the ability to self-reflect and the degree of certainty of a person holds about their self-beliefs; 2) behavioural awareness using the Dysexecutive questionnaire (DEX); 3) clinical awareness (in patients only) using the Schedule for the Assessment of Insight; and 4) metacognitive efficiency relating to both memory and perceptual judgements.

Results from healthy adults revealed a significant negative relationship between age and perceptual metacognitive efficiency, with memory metacognitive efficiency reaching trend levels, and a negative relationship between depression and both measures of metacognitive efficiency. Memory metacognitive efficiency was also associated with memory ability, but no other measures of cognition, and when controlling for age metacognitive efficiency was associated with both cognitive insight self-reflection and self-certainty. There was also an overall association between the two efficiency scores.

A meta-analysis of published FEP data demonstrated an overall significant association between low mood and the cognitive insight measure of self-reflection. There was no significant relationship between either mood or measures of cognition with memory metacognitive efficiency in either clinical group. FEP patients demonstrated a strong association between memory metacognitive efficiency and cognition, where more efficient metacognitive judgements were associated with better memory and higher levels of executive function. ED patients demonstrated a significant positive relationship between memory metacognitive efficiency and independent-rater DEX scores; no relationship was found in the FEP group between memory metacognitive efficiency and any insight scales. Participants in both clinical groups had difficulty successfully completing the perceptual metacognitive task, likely due to its cognitive and executive demands, so successful completion rates were low; therefore results produced by both groups on this measure were less reliable.

Comparing clinical and non-clinical groups (including those with low mood who scored above a cut-off on the Beck Depression Inventory) revealed significant differences in memory metacognitive efficiency; FEP patients had much poorer efficiency than their healthy and depressed peers. Though FEP patients scored lower than depressed individuals in measures of insight, there was little to no difference between scores of FEP and healthy adults on these scales. There was no difference between older healthy adults and ED patients in either their memory metacognitive efficiency or clinical measures of awareness, despite significant differences in actual cognitive abilities. Direct comparisons of clinical groups (ED and FEP) indicated that FEP patients were significantly more aware on clinical insight scales, but there were no between-group differences on the objective memory metacognitive measure. As there is an age related decline in metacognitive efficiency, this lack of difference between the metacognitive efficiency of the clinical groups of interest implies that FEP patients' efficiency may in fact be impaired, whereas it appears to be relatively intact in relation to age for ED patients, suggesting the two patient groups have distinct awareness profiles.

A pilot analysis of structural MR images in a sub-group of patients with early-stage dementia indicated overlapping structural correlates of cognitive insight and metacognitive efficiency overlap with the cortical midline structures (CMS). Anterior cingulate cortex (ACC) and right parietal lobe volumes were positively associated with memory metacognitive efficiency and the volume of both ACC and adjacent subcallosal gyrus were positively associated with self-certainty. Further, there was evidence of a neural dissociation between cognitive insight sub-scales, where prefrontal cortex (PFC) volume was positively associated with self-reflection and negatively with self-certainty. Only the association between self-certainty and subcallosal gyrus volume survived correction for multiple comparisons across the brain volume, likely due to the heterogeneity and relatively small size of this sample.

A clear relationship in healthy adults between increased age and metacognitive decline in both domains of efficiency calls into question the reliability of older adults' self-awareness of daily activity abilities. Evidence for a negative association between objective metacognition and low mood in healthy adults is at odds with the relationship previously observed in clinical samples between low mood and insight, indicating that an association between self-awareness and mood differs between the healthy and patient populations. A significant correlation between memory metacognitive efficiency and cognitive insight scores, when controlling for age, indicates some association between the cognitive and clinical concepts of self-awareness.

Patient behavioural data tells a different story, indicating measures of self-awareness from different disciplines are not as strongly related in clinical groups. Measures of self-awareness across domains appear to have different cognitive correlates, and combined use may not be appropriate in a purely clinical setting. Results also suggest that disordered self-awareness has a different profile across distinct clinical groups. ED imaging data, however, implicates a neural substrate that is common across different domains of awareness in the cortical midline structures.

This thesis provides a framework for understanding the relationship between clinical and cognitive domains of self-awareness on a behavioural and neural basis. The poor overall association between clinical awareness and more objective measures of metacognitive efficiency across groups indicates that the umbrella term “metacognition” refers to a number of loosely associated cognitive concepts that are most closely related at the neural level.

CHAPTER 1

1. DEFINITIONS

METACOGNITION

The term “metacognition” was originally coined by Flavell (1979, p. 906) to describe “knowledge and cognition about cognitive phenomena”. He went on to describe metacognitive knowledge as “[consisting] primarily of knowledge or beliefs about what factors or variables act and interact in what ways to affect the course and outcome of cognitive enterprises” (Flavell, 1979; p907) and that “metacognitive experiences can be brief or lengthy in duration, simple or complex in content... These experiences can also occur at any time before, after, or during a cognitive enterprise.” – Flavell (1979, p908)

Put more simply, metacognition can be referred to as, “thinking about thinking” (Metcalfe & Shimamura, 1994) and is said to involve a combination of knowledge about a process, monitoring of a process and control of a process.

MEMORY METACOGNITION, also termed “metamemory”, refers to knowledge and understanding of memory in general, as well as one’s own memory in particular (Nelson, Narens and Dunlosky, 2004). This knowledge enables individuals to appraise memory demands and to assess available knowledge and strategies in memory.

PERCEPTION METACOGNITION refers to knowledge and understanding about one’s perception, and thus the ability to discriminate between correct and incorrect perceptual decisions.

SOCIAL METACOGNITION refers to the ability to understand one's own thoughts and emotions, as well as the thoughts and emotions of others (Van Donkersgoed et al., 2014). This is associated with "Theory of Mind"; the ability to attribute mental states, such as beliefs, feelings and intents, to other people. Poor theory of mind is associated with poor social function in patients with psychiatric disorders such as schizophrenia (Mazza, De Risio, Surian, Roncone, & Casacchia, 2001).

INSIGHT

CLINICAL INSIGHT, at the most fundamental level, is a broad term used to describe the degree to which a patient with a mental illness understands their illness, with terms and concepts differing across literature and disease (Marková, 2005). In the context of this thesis lack of insight is considered to mean a "lack of awareness of the deficits, consequences of the disorder, and need for treatment" (Amador & Kronengold, 2004, pg5)

Insight is a complex construct with several elements which, when combined, form a rounded self-appraisal regarding one's mental illness. Specifically this refers to the individual's status as a person with an illness, or as one suffering from a disorder that may benefit from a biomedical intervention or treatment. According to David (1990) it has 3 main components:

- Awareness of illness- the general notion that one is suffering from a bio-behavioural change
- Relabeling- the ability to re-label unusual experiences and phenomena as pathological, such as hearing voices
- Compliance- appreciating the need for treatment and agreeing to accept and comply with such treatment.

COGNITIVE INSIGHT is “the ability to self-reflect, to acknowledge the possibility of being mistaken, to be open to feedback, and to refrain from overconfidence” (Warman, Lysaker, & Martin, 2007, p325) and may be measured using the Beck Cognitive Insight Scale (BCIS; Beck, Baruch, Balter, Steer, & Warman, 2004). The BCIS is made up of two sub-scales:

SELF-REFLECTION refers to how much a person is able to reflect on their thoughts. In the case of the BCIS, this term refers to a person’s ability to reflect on whether their thoughts and beliefs about him or herself are correct, or could be changed by someone else’s opinion (Beck et al., 2004).

SELF-CERTAINTY refers to the degree of overconfidence people have in their interpretations of their experiences.

ANOSOGNOSIA refers to a “lack of knowledge of disease”. The term was coined by Babinski (1914) when referring to patients with a lack of awareness of hemiplegia, however it is now used to refer to lack of awareness in other neurological conditions, such as dementia, when referring to lack of awareness of memory (Marková, 2005). The term is often used interchangeably in the dementia literature with insight, and so for the purposes of this thesis all discussion of awareness of psychiatric or neuropsychiatric disorders mental illness will be referred to using the term insight.

SELF-AWARENESS

Self-awareness may be defined as the “the capacity to perceive the ‘self’ in relatively objective terms while maintaining a sense of subjectivity” (Prigatano & Schacter , 1991, p. 13). Moreover, it has been proposed that the capacity to be self-aware is essential to human life, as it facilitates the modification of one’s behaviour to achieve social goals (Stuss & Benson, 1986).

Within this thesis it is to be understood that insight and anosognosia are forms of self-awareness specific to patients' understanding of mental illness.

CHAPTER 2

2. METACOGNITION IN HEALTHY AND CLINICAL POPULATIONS: THEORY AND MEASUREMENT

“At least I know that I don’t know” – Eminem – “Berzerk”

This chapter will outline the basic understanding of metacognition, how it can be measured and how this knowledge can be applied to healthy adults and those with various psychiatric conditions.

As stated in Chapter 1, metacognition can be referred to as, “thinking about thinking” (Flavell, 1979; Metcalfe & Shimamura, 1994). Metacognition is a fundamental aspect of higher cognition in humans (Dunlosky & Metcalfe, 2009) that may support conscious awareness (Koriat, 2007) and social interaction (Frith, 2012). Apart from their subjective experience, a person is said to have good metacognition when their subjective judgements regarding behaviour are accurate. For example, a person with good metacognitive ability may perform poorly on a task but is aware of this low level of performance and rates it as such. Alternatively, a person with poor metacognitive ability would make subjective reports that are not related to their actual performance. This aspect of metacognition can be referred to as “strategic metacognition” (Saxe & Offen, 2010), and will be the focus of this chapter. The term metacognition can also be referred to as “attributive metacognition”, which is a form of self-knowledge where one can attribute beliefs and desires to the self, which is more akin to the concept of cognitive insight, which will be discussed in chapter 3.2.

2.1 METHODS OF MEASURING METACOGNITION

Metacognitive ability (strategic metacognition) can be measured by calculating the accuracy of metacognitive judgements regarding one's performance on a particular task. Accuracy measurements can be split into "absolute accuracy", which refers to the precision of a confidence judgment compared to performance on a task, and "relative accuracy", which refers to the relationship between confidence judgments and performance scores on a task (Maki, Shields, Wheeler, & Zacchilli, 2005). These measurements can be predictive, or made after a task has been completed, and can be obtained using a variety of tasks.

Judgements of learning (JOL; Nelson & Narens, 1990) tasks require participants to make probabilistic judgements about the subsequent recollection of recently learned items. During such tasks, judgments are made regarding how likely the participants believe it is that they will remember the information learned on a later memory test. A typical test requires a learning phase, where participants learn a list of word pairs, and a memory test, in which one word from the pair (cue word) is presented and the second has to be recalled (target word). Participants make JOLs by predicting the likelihood that they will recall the target word during the memory test (Koriat, 1997).

Feeling of Knowing (FOK; Hart, 1965) tasks require participants to make probabilistic judgements about the subsequent recognition of non-recalled information. A typical task asks participants to answer questions about a given topic or recall information recently learned. Questions answered or recalled correctly are set aside, whereas for those answered incorrectly or not at all participants are asked to rate how likely they are to choose the correct answer on a multiple-choice task (Dunlosky & Metcalfe, 2009).

A more objective, experimentally controlled measure of metacognitive ability is achieved by using psychophysical techniques that allow metacognitive judgements to be isolated independently from task performance, thus measuring the relationship between self-appraisal and cognition directly (Fleming & Dolan, 2012; Galvin, Podd, Drga, & Whitmore, 2003; Maniscalco & Lau, 2012). This type of task has emerged much more recently; Fleming, Weil, Nagy, Dolan, & Rees (2010) investigated the metacognitive ability of 31 healthy adults using a two-alternative forced choice (2-AFC) task, where participants were required to make a perceptual judgement about stimuli on the screen and then rate their confidence in their performance on a scale of 1-6 after each trial. This task was unique in that it allowed experimenters to control for participants performance using a staircase paradigm (Levitt, 1971), where the task became easier or harder depending on the participants' abilities, resulting in each participant performing at approximately 70% correct. A similar paradigm was employed by McCurdy et al. (2013) regarding memory, in which participants learned words in the initial phase of assessment, and made a 2-AFC judgement about the word present on the screen during the test phase regarding which of the two words presented was recognised as being from the learned list. Again confidence judgements were made after each trial, however there was no staircase paradigm employed.

2.2 Methods of calculating metacognition

A number of methods have been proposed in the last 60 years to calculate metacognitive abilities, such as absolute and relative accuracy, bias, scatter and discrimination (Schraw, 2009; see table 2.2-1). Such methods can be used to calculate metacognitive ability using tasks discussed previously.

Construct being measured	Outcome measure	Score interpretation
Absolute accuracy	Absolute accuracy index	Discrepancy between confidence judgement and performance. Measures judgement precision.
Relative accuracy	Correlation coefficient	Relationship between a set of confidence judgement and performance scores. Measures correspondence between judgement and performance.
Bias	Bias index	The degree of over- or under-confidence in judgements. Measures direction of judgement error.
Scatter	Scatter index	The degree to which an individual's judgements for correct and incorrect responses differ in terms of variability. Measures differences in variability for confidence judgement for correct and incorrect items.
Discrimination	Discrimination index	Ability to discriminate between correct and incorrect outcomes. Measures discrimination between confidence for correct and incorrect items.

Table 2.2-1. "Five types of metacognitive judgement outcome score" from Schraw (2009), p35.

A problem with absolute measures of metacognition is that abilities can be dependent partly on participants' task performance. For example, Maki et al. (2005) investigated absolute and relative metacognitive comprehension in a group of University students. Participants were required to predict their performance on verbal comprehension tasks, complete the task, and then make judgements about their task performance. Results indicated that metacognitive ability was partly affected by task ability: students with lower verbal abilities made overconfident judgements of future performance on harder tasks and students with better verbal abilities were under-confident in post-task performance judgements. In tasks where participants had revised beforehand all students were overconfident in their performance predictions. Therefore the results demonstrated that absolute accuracy of predictions and confidence judgments depended on students' abilities and task difficulty. Conversely, relative metacognitive accuracy did not depend on verbal ability or on task difficulty.

The most popular method of metacognition calculation in the metamemory literature is the Goodman and Kruskal (1954) gamma statistic (γ), which provides a measure of association, or correlation, between two ordered, symmetrical responses of two or more levels each. Usually used in FOK and JOL studies, participants' performance is related to their pre- or post-task judgements of memory, and is measured at the ordinal level (see figure 2.2-1 for a 2x2 data array).

Type I Primary memory task performance – Correct recognition	**Type II JOL/ FOK**		
	Yes	No	Marginals
Yes	a	b	a+b
No	c	d	c+d
Marginals	a+b	b+d	a+b+c+d=N

Figure 2.2-1 2x2 illustration of potential judgements during an FOK or JOL task, where "a" and "d" are metacognitively ideal responses and "b" and "c" are metacognitively poor responses.

In relation to JOLs such judgements are posed as, for example, "do you think you will remember this word in the recall phase?" whereas for FOK judgements this would be posed as "do you think you will recognise the items you have not recalled correctly?" γ is defined in terms of the frequency of response represented by each of the four cells (a, b, c and d) where:

$$\gamma = \frac{(ad - bc)}{(ad + bc)}$$

The value of γ ranges from −1, which represents that there is 100% negative association between memory and FOK/JOL judgements, i.e. every time a participant gets an answer incorrect they rate a positive FOK/JOL and vice versa, to +1, which represents that

100% positive association between memory and FOK/JOL judgements, i.e. every time a participants gets an answer correct they rate a positive FOK/JOL and vice versa, therefore a value of zero indicates the absence of association between performance and FOK/JOL. Answers closer to +1 indicate good metacognitive abilities; the further individuals deviate from this score the worse their metacognitive abilities are.

Unlike other correlation measures, e.g. Pearson's r or Spearman's rho, γ is unaffected by ties (as it discounts any data where this may occur), which are unavoidable in metamemory research and are otherwise problematic. In addition, no distributional assumptions need to be made for γ (Nelson & Narens, 1990). However, there are a number of limitations to gamma that make it an unreliable measure of metacognition (Schraw, 1995). The most problematic of these limitations is that empty cells greatly distort the observed value of γ. For example, if a participant only makes "a" responses (where they make a correct judgement and accurate appraisal of it) during the task their gamma score will be "undefined" despite a perfect concordance rate between performance and ratings. Further, γ =1 whenever *b* or *c*=0 (i.e. mainly "a" and "d" responses are made) and γ = -1 whenever either *a* or *d* = 0 (i.e. when no "a" or "d" responses are made).

Gamma systematically varies with response bias (e.g. when a participant chooses "Yes" more often than "No" when unsure of the answer, resulting in skewed responses), so that effect artefacts arising from response bias, and not from genuine differences in accuracy, may appear if γ is used as a measure of accuracy (Masson & Rotello, 2009). In other words, if a participant is biased on either a type I or type II response, this can affect γ and thus give an unrepresentative accuracy value. In addition, γ is an asymmetrical test of independence whereby large values of γ suggest that recognition performance on FOK/JOL judgements are related to memory performance. However, when γ = 0 it does not suggest judgements are totally independent of recognition performance (unless using the 2 x 2 judgement method, as shown in Figure 2.2-1). Finally γ values are very sensitive to the distribution of scores along the *ad* and *bc* diagonals; if *a* and *d* are equal the value of γ increases, whereas if they are uneven γ can decrease in value.

Signal detection theory (SDT) allows assessment of discrimination accuracy independent of performance or judgment bias, but its application crucially depends on distributional assumptions. To calculate metacognition using signal detection theory one requires participants to make 1) type I judgements, which are the basic judgement made regarding the primary task (e.g. which stimulus on the screen is brighter, right or left), and 2) type II judgement, which are the basic confidence judgements made (do you think your answer for this trial was: correct or incorrect). Type I sensitivity measures the incorrect rejections, i.e. making a correct answer but saying it is incorrect, or making an incorrect answer and saying it is correct. More correct rejection or correct acceptance during the task results in a better metacognitive score (see figure 2.2-2). However basic signal detection theory still holds a risk of response bias, for example when a participant is unsure of an answer they may tend to answer “a” over “b”, resulting in skewed responses.

Type I Primary task performance	**Type II Self-rated confidence in performance**	
	Confident Correct	Not Confident Correct
Correct Answer	/	x
Incorrect Answer	x	/

Figure 2.2-2 Illustration of judgements required for metacognitive ability to be calculated using signal detection theory, where / indicates the metacognitively ideal response, and x indicates the metacognitively poor response

Most recently Maniscalco and Lau (2012) developed a method of calculating metacognitive efficiency (type II efficiency): “the efficacy with which observers’ confidence ratings discriminate between their own correct and incorrect stimulus classifications” (p. 422), using a computational model grounded in signal detection theory, which removes confounds such as response bias and type 1 sensitivity found in standard signal detection calculations. Their calculations use d-prime (d'), which relates to primary performance on a given task, and meta d' which refers to type 2 sensitivity (confidence in performance). Meta d' represents the level of d' that would have been expected to have generated the observed confidence in performance. For example, if one was confident in their performance on 100% of the trials the expected d' would be 100% correct. This reflects that their measure is one of type 2 sensitivity (meta d') expressed at the level of type 1 signal detection theory (d'). Meta d' can be considered to be a measure of the signal that is available for the subject to perform the type 2 task (Maniscalco & Lau, 2012). Under the ideal observer model we would expect someone with good metacognitive ability to have a meta d' score that = d', i.e their task performance matched the expected result. However, if this is not the case, and meta d'≠ d', participants' type II sensitivity has either out performed or underperformed the expected value. Where meta d' is smaller than d', we can assume that the participant has poor metacognitive abilities.

To calculate metacognitive efficiency, Maniscalco and Lau use the following formula:

$$metacognitive\ efficiency = \frac{meta\ d'}{d'}$$

which controls for the influence of basic task performance on metacognitive judgements (also referred to as meta d'/d'). This estimates the amount of signal strength that is available for metacognition, expressed as a fraction of the amount of signal strength that is available for the primary task. When a participant has 'ideal' metacognitive efficiency they will obtain a ratio score of 1, whereas a participant who has very poor efficiency will obtain a ratio score of 0. Maniscalco and Lau's method isolates subjects' metacognitive efficiency by dissociating a subject- and task-specific metacognitive score (meta d'/d') from both objective task performance and the absolute level of subjective confidence, which both vary on a trial-by-trial basis. In other words, meta d'/d' objectively calculates the efficiency with which a participant is aware of their task performance. Though meta d'/d' relies on assumptions, unlike γ, this measure of metacognition produces an efficiency value which provides the most objective result.

2.3 Healthy adults

Fleming et al. (2010) found large inter-individual variability in metacognitive abilities of healthy young adults, where metacognitive ability varied from 0.55-0.75 (out of a possible 1) despite task performance remaining ~70% correct across participants. In addition, Song et al. (2011) found that participants' metacognitive ability measured in one type of visual discrimination task could predict their metacognitive ability in a second, different visual task, and this effect was independent of the variability in their objective performance on perceptual judgements. Further, to this McCurdy et al. (2013) found that there was a significant relationship between metacognitive abilities as measured on a visual perception task and a memory task, however this was not found by Baird, Smallwood, Gorgolewski, and Margulies (2013). Together these findings suggest that metacognitive ability uses a cognitive process independent of both task used, and, possibly, task domain.

2.3.1 Ageing

Given that there are clear inter-individual differences in metacognitive ability in the healthy younger population, there is some debate as to whether metacognitive ability changes as we age. Some may suggest greater life experience results in better self-understanding and therefore better metacognitive judgements, and there is some evidence to support this. Pliske and Mutter (1996) investigated the awareness of older and younger adults in their general knowledge ability; results showed that older participants were better at predicting whether their answers would be correct or not on a general knowledge test (Dodson, Bawa, & Krueger, 2007; Pliske & Mutter, 1996). Similarly, Vukman (2005) found that accuracy in metacognitive statements regarding problem solving was significantly better in the mature adult group compared to younger adults, with a minor decline in the oldest adult group. Lachman, Lachman, and Thronesbery (1979) found all age groups demonstrated accurate and efficient metamemory, however this may have been related to the finding that there were also no age effects on memory retrieval.

Some research has found there to be no age effect, positive or negative, on metacognitive judgements. This has been found using FOK methodology for face recognition (Eakin, Hertzog, and Harris, 2014) and semantic memory when accounting for subjective accounts of memory awareness (Souchay, Moulin, Clarys, Taconnat, and Isingrini, 2007). Further, Connor, Dunlosky, and Hertzog (1997) also suggest that differences in absolute accuracy are influenced by factors other than on-line monitoring of memory, and demonstrated that, though there were age related differences regarding absolute metamemory accuracy, older adults showed a robust delayed metamemory accuracy that was not significantly different from younger adults. In addition Halamish, McGillivary and Castel (2011) found that, whilst older adults exhibited worse memory performance, they made accurate JOLs where they accurately estimated that they had forgotten more information than their younger counterparts. It was found that both age groups were accurate in predicting their ‘forgetting’, indicating that aging does not impair the ability to monitor forgetting. It has been suggested that studies demonstrating age related decline in JOL’s reflect recall deficits as opposed to a true age related decline in metacognition (Daniels, Toth, and Hertzog, 2009).

Conversely, there is a substantial body of evidence to support the notion that, as with memory (Stuart-Hamilton, 2012), our ability to accurately judge our performance on various tasks also declines with age. This has been demonstrated in a number of study designs, such as forced recall and confidence ratings of words (Kelley & Sahakyan, 2003; Weil et al, 2013) and pictures, despite controlling for memory ability (Pansky, Goldsmith, Koriat, and Pearlman-Avnion, 2009). Work by Huff, Meade, and Hutchison (2011) has also demonstrated that older adults recalled intrusions with greater confidence than young adults, indicating that the older adults had less awareness that their recall was incorrect. There is evidence of an age related decline in FOK accuracy (Cosentino, Metcalfe, Holmes, Steffener, and Stern, 2011), however it has been suggested this age effect is only the case in episodic, and not semantic, memory (Souchay et al., 2007). Regarding JOLs, Tauber and Dunlosky (2012) studied effects of age on emotional word learning and found that, though younger adults were more sensitive to learning ability of positive words versus neutral words, older adults were not, and both were sensitive to learning negative words. Toth, Daniels, and Solinger (2011) found that only younger adults benefited from prior knowledge on the recognition tests, whereas this appeared to interfere with the familiarity of pictures shown to older adults and reduced accuracy of the memory predictions. Age-related reductions in metamemory accuracy may also be affected by deficient recall and monitoring of stimuli details such as colour and font size (Wong, Cramer, & Gallo, 2012), where older adults were found to be better at picture recall than colour recall, and font size also had an impact. Soderstrom, McCabe, and Rhodes (2012) found that, using both Judgements of Remembering and Knowing (JORKs)– where participants predicted whether learned word pairs would be remembered (i.e. recalled) known (i.e., be familiar but not recalled), or forgotten – older adults demonstrated poor accuracy compared to actual memory ability, where they were overconfident in their prediction of remembering.

Some evidence suggests older adults require extra time to reach similar performance levels as their younger counterparts (Thomas, Bonura, Taylor, and Brunyé, 2012) however when given the opportunity to allocate time between tasks of varying difficulty, unlike younger participants, older adults allocated even amounts of time regardless of task difficulty (Froger, Sacher, Gaudouen, Isingrini, and Taconnat, 2011), indicating a reduced awareness of the need for extra time. Bender and Raz (2012) found that older adults consistently used ineffective encoding strategies, further indicating older adults have poor awareness of their memory abilities.

Despite different study designs there is a clear, large body of evidence support the idea of an age related decline in metacognition regarding task performance, as opposed to research demonstrating no such trend. However evidence suggests there may be variations in the age effect, where awareness of general knowledge and problem solving ability may improve with age, and other cognitive domains such as awareness of task performance and daily functioning may decline over time. Indeed, there is evidence to suggest that awareness of deficits in both questionnaire assessments of daily life and laboratory based task performance are related, and decline as we age (Harty, O'Connell, Hester, & Robertson, 2013). These findings are more consistent with real-world reports that lack of awareness of cognitive, physical and perceptual abilities in healthy older adults can be problematic, with aberrant confidence leading to dangerous or even life threatening behaviours. Hultsch, MacDonald, Hunter, Levy-Bencheton, and Strauss (2000) demonstrated that there are notable changes in self-appraisal as we age, and these tend to centre on inaccuracies regarding beliefs about cognitive ability and control over cognition. Older adults tend to demonstrate increased over-confidence compared to actual performance when compared to younger adults (Dodson et al., 2007; Light, Singh, & Capps, 1986), which has been supported by research regarding "real-world" examples of age-related decline in awareness of driving ability (Ross, Dodson, Edwards, Ackerman, & Ball, 2012). Older adults between the ages of 65–87 years old were asked about their driving abilities, and it was found that, regardless of previous accident history, 85% of the drivers in this age range rated themselves as "good" or "excellent" drivers. In addition, there was no change in rating with age despite finding a correlation between increased number of accidents and older age.

Metacognition can operate across numerous domains of cognition, such as perception and memory. In addition, metacognitive judgments can be prospective (such as a prediction of success) or retrospective (such as confidence in past choices). Research has emphasized conceptual similarities between some characteristics of memory metacognition and executive functions (Shimamura, 1995; Fernandez-Duque et al., 2000; Souchay, Isingrini, & Espagnet, 2000; Pannu and Kaszniak, 2005). However, the domain-specific characteristics of metacognition are not well explored. McCurdy et al. (2013) showed that metacognitive ability in perceptual and mnemonic domains were moderately but significantly related in a sample of young adults. Whether aging affects metacognition in a domain-general or domain-specific fashion is not clear from the previously reported literature. A study by Perrotin, Belleville, and Isingrini (2007) compared patients with mild cognitive impairment (MCI) to healthy age matched controls in their FOK abilities looked at the effects of tests of executive function. Results indicated that there were between-group differences; highlighting that FOK accuracy was primarily related to memory abilities in people with MCI, as opposed to control participants, in whom it was related to executive functioning.

However, it has been difficult to separate metacognitive ability from age-related changes in performance. As mentioned in section 2.1.1, the sensitivity of metacognitive measures used in the previously reviewed literature is often inherently affected by task performance itself, which can also be affected by age (Stuart-Hamilton, 2012). If we are able to remove the effect of performance on metacognition we may see a difference in metacognitive efficiency across the lifespan and cognitive domains (see 2.3.2).

2.3.2 Relationship to brain structure and function

Research has revealed a specific neural basis for strategic metacognitive ability in human prefrontal and parietal cortices (Saxe & Offen, 2010). The study by Fleming et al. (2010) referred to in section 2.3 demonstrated that the inter-individual differences noted in metacognitive ability were also significantly associated with gray matter volume in- and white matter microstructure connected with - the anterior prefrontal cortex (aPFC) volume, where greater volume was associated with better metacognitive ability. Fleming, Huijgen, and Dolan (2012) investigated metacognitive aspects of decision-making and found that during an fMRI task the right rostrolateral prefrontal cortex (rlPFC) showed greater activity during confidence reporting compared to a matched control condition. Greater activity in this area was also significantly associated with reported confidence in task performance where the strength of the relationship between activity and confidence predicted metacognitive ability across individuals. In addition, functional connectivity between right rlPFC and both contralateral PFC and visual cortex increased during metacognitive reports. McCurdy et al. (2013) found a similar association to previous work between the volume of the aPFC and visual discrimination metacognitive abilities, with an additional weak correlation with precuneus volume. Memory metacognitive abilities, however, were only correlated with precuneus volume. It is suggested that the joint association of metacognitive abilities in different domains and the precuneus explain the behavioural correlation between metacognitive tasks of memory and perception. Further, a recent study by Baird, Cieslak, Smallwood, Grafton, & Schooler (2014) investigated the association between white matter connections and metacognitive accuracy. Results demonstrated that accuracy on perceptual metacognitive tasks were associated with white matter connections to the ACC, whereas accuracy for memory metacognitive judgements were associated with white matter extending into the inferior parietal lobule, indicating that there are distinct neural correlates across metacognitive domains. Yokoyama et al. (2010) also investigated the functional neural correlates of metacognitive abilities in a memory task using fMRI; they found increased activity in the posterior-dorsal right frontopolar cortex when confidence ratings about task performance were better correlated with actual memory performance, i.e. when better metacognitive judgments were made.

Further to this, Baird et al. (2013) used resting-state functional connectivity (rs-fcMRI) to relate intra-individual variability in metacognitive judgements noted in previous studies to the connectivity of the medial and lateral regions of aPFC, to identify if specific anatomical parts of the aPFC are specialized for domain specific metacognitive processes. Akin to previous research they report a behavioural dissociation in perceptual and memorial metacognitive judgments. Functional connectivity analyses indicated that distinct patterns of connectivity were associated with individual differences in both perception and memory metacognitive abilities. As with previous studies, greater connectivity was observed during perceptual metacognitive judgments between the lateral aPFC and the right dorsal anterior cingulate cortex (dACC), bilateral putamen, right caudate, and thalamus. Similarly to previous work they identified that memory metacognitive ability was associated with greater connectivity between medial aPFC and the right central precuneus and intraparietal sulcus/inferior parietal lobule. In addition to metacognitive judgements about 'basic' cognitive processes such as perception and memory, De Martino, Fleming, Garrett, & Dolan (2013) asked participants to make choices between two snack items, where they were required to choose the most expensive item, and then rate their confidence in this value-based choice. Results indicated that accuracy of confidence judgements are positively associated with functional connectivity in the ventro medial PFC (vmPFC), suggesting that the frontal lobes mediate metacognitive judgements across a number of domains.

These results are supported by brain stimulation studies. Rounis, Maniscalco, Rothwell, Passingham, and Lau (2010) used transcranial magnetic stimulation (TMS) to bilaterally reduce activity in the DLPFC whilst participants carried out a visual discrimination task. Reduced activity in the targeted area of the PFC was associated with reduced metacognitive judgements with signal detection theory analysis confirming this was due to a reduction in metacognitive ability, not response bias. Further to this point, Harty et al. (2014) tested the awareness of older adults to correctly detect performance errors; after anodal transcranial direct current stimulation (tDCS) was performed over the right DLPFC they reported that participants displayed a significant increase in error detection, but not performance accuracy, indicating that performance and metacognition can be dissociated. This sample consisted of older adults (65-86 years old) and thus further implicates the frontal lobes in the executive-ageing theory of metacognitive decline as we age (2.3.1).

There is also evidence from lesion studies. Hoerold, Pender, and Robertson (2013) demonstrated that patients with lesions to the left and right frontal lobe had impaired metacognitive awareness. Further, a recent study by Fleming, Ryu, Golfinos, and Blackmon (2014) compared metacognitive efficiency in patients with lesions in the aPFC and found that, compared to healthy adults and control patients with temporal lesions, aPFC lesions lead to a selective deficit in perceptual metacognitive efficiency (meta d'/d'). As these regions are susceptible to aging-related atrophy (Fjell et al., 2009) it is plausible that there are age-related changes in metacognitive ability. However it is unknown how aging affects metacognitive ability when dissociated from the confounding influence of task performance.

Studies have also looked into self-reflection, an introspective aspect of metacognition, in healthy adults. Activation in a distinct area in the frontal lobe, the medial PFC (MPFC), was found to be associated with participants' subjective judgements of their personality traits, current mental state, and physical attributes (Jenkins & Mitchell, 2011). Authors suggested that, though each type of self-reflection was also associated with unique areas of activation, self-referential thought clearly utilises a cognitive processes that is related with the MPFC. This area is also associated with implicit self-referential thinking; Rameson, Satpute, & Lieberman (2010) studied a group of participants who associated themselves as "scientific" or "athletic" (referred to as their schema) and asked them to rate a number of words on how representative they were of the respective categories. Though the task was not explicitly self-reflective in nature, participants had faster response times for words matching their personal schema (i.e. participants who saw themselves as scientific responded faster to scientific words). During an fMRI task, the explicit referential task required participants to rate whether a schematic word described them by rating it “me” or “not me”. The implicit task required participants to rate whether scientific or athletic photos had people in them. Again, though this task was not self-referential, areas of the precuneus PCC, vMPFC, MPFC, ventral striatum, and subACC showed significant activation, which were also active in the explicit task. These results demonstrate that activation of frontal structures occurs when observing words or pictures one views as self-referential, even if this is not the primary task being undertaken.

There is therefore a great deal of behavioural and brain imaging evidence, in a number of domains, to indicate that there is an age related decline in metacognitive abilities from early to older adulthood. Indeed, there is also a large body of evidence that demonstrates an age-related decline in frontal lobe volume, where both the gray matter and white matter connections are affected (Cabeza & Dennis, 2013). Specifically, cross-sectional studies have indicated that pre-frontal cortex atrophy is affected to a greater degree as we age, compared to other cortical regions, with the gray matter in the lateral PFC regions demonstrating the sharpest decline (Raz, 2000, 2004). Longitudinal studies have further supported this notion (Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003) and indicated that the PFC shows a steeper decline as we enter older age. Further, studies across a number of domains have implicated that the neural basis of metacogntion is located in the frontal lobes and CMS (Fleming & Dolan, 2012).

2.3.3 Emotion

Recent evidence also suggests that emotion can affect metacognitive abilities. Massoni (2014) used a similar computerised paradigm to other recent studies mentioned in section 2.3 to investigate the effect of worry on metacognitive efficiency. Participants had to complete a 2-AFC task that required a perceptual judgement about which of two circles contained more than 50 dots. There was a betting phase prior to the perceptual task that required participants to bet money (€20 or €200) on the likelihood of their success over the next 2,3 or 4 trials, with the higher stake bet designed to induce anxiety, and betting on more trials would also induce higher anxiety. Before the perceptual trial participants rated their level of anxiety on a scale of 0-9, participants then completed a perceptual trial and immediately after rated their confidence in their performance. Maniscalco and Lau's (2012) Meta-d' was used to calculate metacognitive efficiency, and results demonstrated that higher anxiety led to improved metacognitive judgements on this task, implicating emotion in the accuracy of metacognitive judgements.

2.3.4 Healthy adults – conclusions

There is a great deal of behavioural evidence to suggest that there are inter-individual differences in the metacognitive abilities of healthy adults, and that abilities also reduce as we age. Imaging studies have indicated that this variance is associated with gray matter volume in the frontal lobes and the CMS. Support for the association between age and metacognitive decline comes from imaging studies which indicate atrophy of the frontal lobes is significantly associated with age, especially when entering older age. Evidence also suggests that there is an association between metacognitive abilities in different cognitive domains. Further, the current literature can be combined to suggest that there is a neural basis of metacognitive function focused in the frontal lobes.

2.4 Metacognition in psychiatric populations

As covered in Section 2.1, metacognition in healthy adults may be mediated by frontal lobe function. It has therefore been suggested that metacognition may be impaired in neuropsychiatric disorders in which frontal lobe function is thought to be compromised and in which structural imaging has suggested reductions in frontal lobe volume (David, Bedford, Wiffen, & Gilleen, 2012), or damaged (Fleming et al., 2014; see Chapter 2.3.2).

Mainly using FOK and JOL methodology, metacognitive abilities have been measured in both dementia (chapter 2.4.1) and psychosis (chapter 2.4.3).

2.4.1 Dementia

Dementia (including Alzheimer's disease [AD] and other disorders) is a neurological syndrome primarily characterised as affecting memory with other cognitive functions also involved, resulting in a steady decline in functioning profiles as the disorder progresses. Mild cognitive impairment (MCI), where cognitive impairment exists but not to the extent of causing significant functional impairment, often precedes overt dementia. However there is a large amount of heterogeneity regarding areas of cognition affected under the umbrella term of dementia. As will be further outlined in Chapter 3, anywhere from 20-80% of patients with MCI and dementia have reduced awareness of their cognitive impairments (Derouesne et al., 1999; Reed, Jagust, & Coulter, 1993), which can negatively impact on treatment adherence, and the life satisfaction of both patient and caregiver (Rymer et al., 2002). However, like functioning profiles, there is also a large amount of heterogeneity regarding patients' awareness of their cognitive deficits (Cosentino & Stern, 2005). Variance in results on metacognitive abilities in patients with dementia may come from the measures used to assess patient awareness; much of the literature in this field has relied on clinician ratings and clinician- or caregiver-patient discrepancy ratings (global measures) for assessments of patient awareness of functioning, which are often questionnaire-based and can be subjective in nature. Though these scales are often related to actual functioning (local functioning, e.g. performance on a memory task) more recently research has focussed on developing measures of self-awareness that are more objective, such as FOK and JOL (as described in 2.1), which have been shown to have different correlates to global measures of awareness.

Another explanation for the heterogeneity across tasks comes from a review of metamemory in patients with dementia by Souchay (2007), who concluded that there was a fractionation of memory metacognition in this patient group, whereby some abilities, such as short-term self-knowledge updating and cue recognition, are preserved, and others degrade faster than the normal rate of ageing, such as long-term self-knowledge and episodic memory updating. This is also called “mnemonic anosognosia”; at the beginning of a memory metacognition test the patients have “forgotten that they forget”, and make predications and judgements on their memory performance based on this erroneous self-knowledge. However, after completing a few blocks of trials, patients’ self-knowledge is updated to integrate information about their poor memory performance and they are more accurate at rating their performance. Agnew & Morris (1998) proposed, using their Cognitive Awareness Model (CAM), that initial judgements may improve over a short period of time in patients with dementia on JOL tasks, as self-knowledge is updated to match experience and performance, therefore resulting in more accurate self-judgements over a short period of time. Moulin, Perfect, and Jones (2000) demonstrated that patients with dementia have intact short-term memory monitoring, and that they show similar responses to healthy older adults in relation to stimulus parameters that increase or decrease the ability to recall information in such tasks, such as recall tasks compared to recognition, item difficulty and distinctiveness. Results therefore suggest that their lack of awareness of memory and cognitive deficits is not related to “primary anosognosia”, however, due to their mnemonic anosognosia, there is no consolidation of this information, leading to patients forgetting and poor self-judgments resuming after a time. Indeed, Ansell and Bucks (2006) demonstrated that, despite short-term improvement in JOLs over three trials, patients’ JOL accuracy reverted back to baseline after a break of only 20 minutes. Thus, this phenomenon has been termed the “petrified-self”, wherein the patient’s long-term self-knowledge is unchanged from a time before they were experiencing these memory problems, and judgments on anticipated task performance are made using this out-dated information. Further, Gilleen, Greenwood, Archer, Lovestone, & David (2011) investigated the relationship between clinical awareness and discrepancy scores using the Memory Awareness Rating Scale (MARS; Clare, Wilson, Carter, Roth, & Hodges, 2002) and Rivermead Behaviour Memory Test (RMBT; Wilson, Cockburn, & Baddeley, 1985). Patients with low RMBT scores rated their memory as better than patients who scored higher; those with higher scores were more accurate at rating their memory abilities, however they still underestimated their deficits. In addition, Souchay, Isingrini and Gil (2002) found that FOK judgements were more strongly related to memory than to executive function in AD patients, but to executive function in healthy, age matched controls. These findings may help develop our understanding of metamemory, as it is this process that is crucial for accurate introspective judgements.

It has been suggested that more objective, experimentally controlled measures of metacognition should be used in research, which in turn will help us understand the specific nature and mechanisms underlying such processes and why they sometimes go wrong. A review by Cosentino (2014) found that over time there has been an increase in the number of studies using objective task paradigms in the field of dementia research, however to date these tend to use biased statistical methods, such as the gamma statistic (described in section 2.2; Cosentino, Metcalfe, Butterfield, & Stern, 2007).

2.4.1.1 Relationship with mood

Though most work in relation to memory awareness in dementia and mood has been carried out using clinical scales (see chapter 3.1.3.1), there is some evidence to suggest that more objective measures of memory metacognitive function are associated with mood.

Nakaaki et al. (2008) investigated the relationship between depression and the number of words AD patients predicted they would recall, where they found that patients with depression were significantly more accurate in the number of words they would recall compared to patients who were not depressed, independent of actual memory ability. Similarly Gilleen, Greenwood, Loveston and David (2011) found that a MARS measure of prediction memory accuracy, but not post-diction, was associated with depression scores, where lower mood was associated with better prediction. There was no significant association with post-task memory judgements and mood, which may be due to the observation that immediate JOLs made by patients with dementia are generally more accurate than predictions (discussed in section 2.4.1), where most patients make more accurate short-term ratings. It may be that mood is associated with long-term memory ability but does not affect short-term post-diction judgements when memory has been updated temporarily (according to the CAM model).

2.4.1.2 Relationship to brain structure and function

There is a substantial body of evidence to suggest that the observed lack of accurate memory metacognition in dementia is related to reduced volume and function in the frontal lobes. For example, Souchay, Isingrini, Pillon, & Gil (2003) found that patients with frontotemporal lobe dementia (FTD) were worse at self-ratings on memory test compared to patients with AD, which the authors suggest is related to the increased frontal deficits observed in patients with FTD.

A meta-analysis of neural correlates of self-referential processing in healthy subjects has demonstrated that there may be three clusters within the CMS that are specialized in different self-referential processes (Northoff et al., 2006). The ventral region (medial orbitofrontal cortex, ventromedial PFC, and subgenual and pregenual ACC) was identified as labelling stimuli as self-referential; the dorsal region (dorsomedial PFC and supragenual ACC) was identified as evaluating self-related stimuli; and the posterior region (posterior cingulate cortex [PCC], retrosplenial cortex, and medial parietal cortex) was identified as helping to place "self-related" stimuli in temporal cortex and linking them with previously self-related stimuli. Additionally, this relationship was found regardless of stimuli type, such as emotional or memory.

2.4.2 *Schizophrenia*

The notion of metacognition has also been investigated in patients with schizophrenia, however this has primarily been studied regarding "social" aspects of metacognition using questionnaires, interview methods and analysis of "self" narratives (Lysaker et al., 2005). Results from this field of research have indicated that there is a relationship between "social metacognition" and improved insight, better executive function and social function. However, less work has been carried out to investigate the more objective, experimentally controlled aspects of metacognition in patients with schizophrenia.

Using FOK methodologies has produced mixed results. Bacon, Danion, Kauffmann-Muller, and Bruant (2001) asked schizophrenia patients and age matched controls to perform a recall task, where they were asked to rate their confidence after each recall, and make FOK ratings for words they had not successfully recalled. Results demonstrated that, despite patients having worse recall compared to healthy controls, their confidence ratings for recall and accuracy of confidence ratings and FOK judgements did not differ from those of the control group, however FOK ratings themselves were significantly reduced for patients with schizophrenia. Additionally, discordant FOK judgements were also made more frequently in the patient group. However Souchay, Bacon, and Danion (2006) found no difference between patient and control FOK judgements, bias or discrimination, as calculated using the gamma statistic.

2.4.2.1 *Relationship with neurocognition, mood and insight*

Research by Lysaker et al. (2005) has indicated that there is a relationship between self-report and narrative measures of metacognition and executive function in patients with schizophrenia. It is suggested that a deficit in neurocognition is associated with poor metacognitive function as the reduced set shifting ability can lead to poor self-monitoring, or indeed poor memory can lead to inability to up-date self-knowledge (Dimaggio & Lysaker, 2010). However, recent research has indicated that this relationship is moderated by disorganized symptoms, where increasing disorganization results in a stronger association between executive function and neurocognition (Minor & Lysaker, 2014).

An association has also identified between understanding ones' own mind and depressed mood (Lysaker et al., 2005), where presence of depressive symptoms were related to better self-understanding. Further, there was also an association with metacognition and insight into illness, however this research was conducted using self-report assessments of metacognition as opposed to the more objective measures described in section 2.1. Conversely, a study by Morgan & David (2010) indicated that, although some patients displayed poor metacognitive processing of their unusual cognitive experiences (as assessed by qualitative analysis of a clinical insight schedule), this was not directly associated with a failure to acknowledge or recognise, even superficially, that they were experiencing psychological change or suffering from a mental illness.

A more objective measure of metacognitive function was developed for use in groups of patients with schizophrenia (Koren et al., 2004), comprising a metacognitive version of the Wisconsin Card Sorting Test (WCST). Patients were asked to give a "forced" response, i.e. perform the WCST as normal, and additionally they gave a "free" response, where they had to rate their confidence in their performance (where 0= just guessing, and 100= completely confident) in each trial, and choose if they wanted that trial to "count" towards their final score and overall performance, in which case they received a 10 cent bonus for each correct trial, and a 10 cent penalty if incorrect. Results demonstrated that the metacognitive ratings (confidence and whether trials counted towards the final score) were associated with insight into illness more so that original WCST scores, therefore indicating that though insight is associated with executive function, it is more strongly associated with self-awareness of thought processes.

It is clear that more experimentally controlled research into metacognitive function is required in this patient group to confirm whether it is associated with executive function and insight into illness, as is suggested by the qualitative evaluations of self-narratives.

2.4.2.2 Relationship to brain structure and function

Most neuroimaging research regarding self-awareness in schizophrenia patients has been related to clinical measures (Chapter 3.2.3) and has found significant associations with the functional activation in Cortical Midline Structures (CMS; Murphy et al., 2010; van der Meer, Costafreda, Aleman, & David, 2010) and volume of the frontal lobes (David et al., 2012; see Chapter 2.3.).

Bedford, Surguladze, Giampietro, Brammer, & David (2012) carried out a study into the functional correlates of self-evaluation in relation to positive, negative and illness related words in patients with schizophrenia and healthy adults. Results indicated that patients demonstrated a hypo-activation in both the medial superior frontal gyrus (DLFPC) and posterior cingulate, compared to controls, across the evaluation of all traits. Further, inverse correlations with insight were noted in the ACC as well as frontal and parietal regions. Murphy et al. (2010) investigated the functional correlates of self- versus other- (in this case a close other) evaluations using positive and negative emotionally valenced words. There was significant activation observed in the medial prefrontal and posterior cingulate cortices during self-evaluation trials for both patients and healthy controls, however there were no between-group differences identified, possibly due to lack of power as the result of a small sample size (11 patients and 10 controls). In addition, there was significantly reduced activation observed in patients compared to healthy controls in the right middle frontal gyrus when considering other-evaluations. Finally, similar relationships have also been seen in non-clinical populations (Modinos, Renken, Ormel, & Aleman, 2011). Across a group of students with a varying degree of schizotypal traits (a measure of psychosis-proneness), fMRI indicated that making self-referential judgements (vs. other or semantic judgements) induced activation of the CMS. When comparing participants with high psychosis-proneness to those with lower scores, there was a significantly increased degree of activation in the CMS and frontal lobes for self-judgements of positive and negative personality traits in higher scoring participants, indicating that atypical activation in these regions may be risk factors for psychotic illnesses.

2.4.2.3 Training

Metacognitive training is already being trialled in psychosis patients (Aghotor, Pfueller, Moritz, Weisbrod, & Roesch-Ely, 2010; Favrod, Maire, Bardy, Pernier, & Bonsack, 2011; Pijnenborg, Van der Gaag, Bockting, Van der Meer, & Aleman, 2011) and has been shown to produce improvements in the domain of clinical insight (Pijnenborg et al., 2014). Metacognitive training developed by Aghotor et al. (2010) involves highlighting common "cognitive distortions" (atypical attribution styles, jumping to conclusions, lack of mental flexibility, need for closure, overconfidence in errors and negative cognitive schema), making patients aware of them and then asking them to reflect and critical evaluate them, with the view to changing them, thus changing their method of problem solving. Another form of metacognitive therapy has been developed by Van Donkersgoed et al. (2014), "Metacognitive reflection and insight therapy" (MERIT), which is manual-based and personalised to each individual patient. This treatment is target driven as opposed to following a set course of therapy sessions and aims to stimulate Lysaker's (2005) four elements of metacognition (self-reflectivity, understating the others' mind, decentration and mastery). Patients are encouraged to produce a personal narrative so therapists can identify errors in their metacognitive thinking and help patients reflect on themselves and others in more complex ways. No data have been published on the outcomes of this therapy to date.

2.4.3 Clinical populations - conclusions

There has been a reasonable amount of research into the metacognitive abilities of clinical groups in comparison to healthy controls, particularly in dementia but also in schizophrenia patients, and this tends to be in the memory domain as opposed to other aspects of cognition. That said there is evidence from behavioural and imaging studies that patients with dementia and FEP display a reduced ability to monitor their memory abilities accurately, and this tends to be related to the frontal lobes. Further evidence has demonstrated that there are also deficiencies in patient populations regarding self-reflection. Neural correlates of self-reflection in patients samples are similar to those identified in in healthy adults, and may be implicated in clinical awareness (see chapter 3). Evidence from schizophrenia patients has shown that it is possible to improve metacognitive accuracy with training in the form of group cognitive remediation therapy.

2.5 Conclusions

It is clear that there is a growing body of evidence that suggests there is a reduction in metacognitive ability, both in health ageing and in clinical syndromes such as dementia and schizophrenia, all of which have been investigated using similar experimentally controlled methodologies. Deficits and individual variation in metacognitive abilities have been linked to reduced volume, connectivity and functioning in the frontal lobes in healthy controls and patients. There has also been recent evidence from schizophrenia research to suggest metacognitive function can be improved using a form of cognitive remediation therapy that addresses cognitive biases. Whether this is also the case for dementia patients is yet to be investigated.

It has been suggested that "lab based" research cannot apply to the "real world" deficits that patients experience, and this may be why we find contradictory or non-significant results when comparing the two (Lysaker, 2010). This may especially be the case in patients with schizophrenia, wherein their primary deficit is not one of memory, but cognition in general. Metacognition research in healthy adults appears to have broadened from basic cognition and psychophysics and is working towards more socially oriented concepts. On the other hand, clinical research has focussed on complex social concepts of metacognition from the beginning, where deficits are commonly uncovered, but work using more fundamental psychophysical measures is lacking. An attempt to address this will be made in this thesis.

CHAPTER 3

3. INSIGHT AND LACK OF AWARENESS IN CLINICAL DISORDERS: PSYCHOSIS AND DEMENTIA

> "Insight is not a word of plain and single meaning." - Aubrey Lewis, 1934 p.332

> "I'm not crazy! My mother had me tested!" Sheldon Cooper – "The Big Bang Theory"

3.1 CLINICAL INSIGHT

As stated in chapter 1, at the most fundamental level clinical insight refers to an aspect of self-awareness related to illness and symptoms. In the context of this thesis it refers to a patient's level of awareness, or un-awareness, of their mental illness. It is often described as an illness-specific domain of metacognitive function, where metacognitive deficits are associated with a number of neuropsychiatric disorders (David et al., 2012), including first episode psychosis (FEP), schizophrenia and dementia. The term "lack of awareness" is often used interchangeably with "anosognosia" in neurology and in dementia and Alzheimer's disease (AD) research, where anosognosia refers to a "lack of awareness of deficits" such as reduction in memory and cognitive abilities, as opposed to the unawareness that experiences such as hallucinations are in a sense 'not real' and symptoms of a disorder. In this thesis "lack of insight" will refer to the multi-dimensional framework of unawareness of illness in clinical populations (see section 3.1.1 for further details).

3.1.1 CONCEPTUALISATION

Historically, insight was considered to be an all or nothing phenomenon (Lewis, 1934), where a patient either possessed awareness of their illness, or they did not. Now it is considered to be a multi–dimensional construct, where patients can demonstrate various levels of awareness of their illness, which may change over time. Insight is normally conceptualised and measured in terms of awareness of the clinical aspects of the disease –

such as awareness of having schizophrenia or dementia, of symptoms and the need for treatment. These dimensions show some differentiation and have been shown to be somewhat independent of one another in both disorders (David, 1990; Starkstein, Sabe, Chemerinski, Jason, & Leiguarda, 1996). Gilleen, Greenwood & David (2011) found that insight into symptoms, behaviour and cognition were to some extent isolated, and each was predicted by different factors, highlighting that it is a complex and possibly modular concept. Indeed, it is possible for patients to be aware of some deficits but not others (Clare et al., 2011).

The nature and degree of awareness that psychiatric patients have about their illness has important implications as poor insight can result in later detection of illness, poorer treatment adherence and poorer outcomes (Amador & David, 2004; Cosentino & Stern, 2005; Kemp & David, 1996; Lincoln, Lullmann, & Rief, 2007) and may impact negatively on the life satisfaction of both patient and caregiver (Rymer et al., 2002). It has been reported that around 50% of patients with schizophrenia and other psychotic disorders have poor insight (Arango & Amador, 2011), where the awareness that different symptoms are pathological can vary from 30% (hallucinations and thought disorder) to 50% (delusions). Further, Lambert et al., (2010) report that during an initial 18-month treatment period of FEP patients, only 34% patients were fully adherent to treatment, 47% had at least one phase of noncompliance, and 19% persistently refused treatment. In patients with dementia it has been reported that between 20% and 80% of patients are not aware of their cognitive and behavioural symptoms, depending on severity and measures used (Reed et al., 1993).

It appears that in both disorders there are specific errors in “self” awareness and monitoring, as opposed to “other”, which again implies the two types of awareness are modular and potentially separable constructs. For example, Zamboni et al. (2013) asked patients with AD and mild cognitive impairment (MCI), as well as controls, questions about themselves and a significant other, and created discrepancy scores using the significant others' response. Results showed that that AD patients were less accurate than those with MCI and controls relating to "self" but not "other" questions, as demonstrated by much larger discrepancy scores.

3.1.2 Clinical insight in schizophrenia

3.1.2.1 Relationship with psychopathology

Lack of insight has been reported to be a characteristic feature of psychotic disorders (Amador et al., 1994). The degree of insight into illness is also associated with the severity of other prominent symptoms. A meta-analysis by Mintz, Dobson, and Romney (2003) analysed the relationship between insight and the 4 main symptom domains of schizophrenia; global, positive, negative and depressive.

An analysis of 19 studies found that as global symptoms increased, degree of insight into illness reduced. Further, it was calculated that variance in global symptoms explained 7.2% of the variance insight. This significant relationship was also found to hold across all conceptual domains of insight: awareness of mental disorder, awareness of social consequences, awareness of need for treatment, awareness of symptoms and attribution of symptoms.

An analysis of 22 studies found that positive symptoms, such as hallucinations and delusions, were also a significant predictor of insight. Here an increase in positive symptom severity was associated with worse insight, whereby 6.3% of the variance in insight can be explained by variance in positive symptoms. This relationship held across all domains of insight. An analysis of 20 studies found that, as severity of negative symptoms, such as flat affect and lack of motivation, increased so degree of insight into illness reduced. Approximately 5.2% of variance in insight can be explained by variance in negative symptoms. This effect held across all insight domains except for awareness of symptoms.

Finally, evidence suggests that low mood is a predictor of good clinical insight (Mintz et al., 2003; see Amador and David, 2004 for review) and higher levels of depression at first admission predict higher levels of insight at 3 year follow up (Saeedi, Addington, & Addington, 2007). Analysis of 15 studies revealed a slightly smaller but highly significant relationship between low mood and improved illness awareness was evident, where 3.2% of insight variance is explained by variance in depression. This effect also held across all domains of insight. Equally, abnormally elevated mood alongside psychosis has been associated with poor illness awareness (Sanz, Constable, Lopez-Ibor, Kemp, & David, 1998). Further, it has been demonstrated that patients diagnosed with their first episode of psychosis who score highly on ratings of mania had significantly less awareness of a need for treatment than those with low mania scores (Morgan & David, 2010). Additionally, patients with bipolar disorder experiencing a period of mania were found to have an increased likelihood of poor illness awareness (Amador et al., 1994). The concept of "depressive realism" has been used to explain to this mood-insight relationship, whereby low mood results in a person holding a more accurate view of themselves and the world (Ackermann & DeRubeis, 1991; Haaga & Beck, 1995) or reduced self-serving bias, where a person blames external factors for their misfortune, which in turn leads to improved awareness of illness. Cavelti, Beck, Kvrgic, Kossowsky, & Vauth (2012) carried out a cross-sectional analysis of the relationship between insight and psychopathological symptoms, with results demonstrating the common observation that higher reported levels of insight were associated with increased levels of depression. The analysis went on to demonstrate that that the relationship between depression and insight was positively mediated by patients understanding of their illness as being disabling to social function and chronic, and was reduced by an expectation that symptoms could be improved by treatment. The association between insight and depressive symptoms was also further reduced in patients who held a positive attitude to recovery.

However it should be noted that, combined, the relationship between these four main areas of psychopathology and insight into illness only explain 21.9% of the variance, thus indicating that there are other factors that influence the degree of insight patients possess about their illness.

Insight can also predict clinical outcomes. A longitudinal analysis by Mohamed et al., (2009) indicated that baseline clinical insight was significantly associated with levels of schizophrenia symptoms at 18-month follow-up, where better insight resulted in lower symptom severity, and Capdevielle et al., (2013) reported a small but significant positive association with insight and remission of other clinical symptoms. Further, Austin et al. (2014) demonstrated that self-reflective or 'metacognitive beliefs' about illness are better predictors of illness course than depression or anxiety.

3.1.2.2 Relationship with neuro-cognition

An area that may also explain variance in patients' insight variance is neuro-cognition. A meta-analysis by Aleman, Agrawal, Morgan, and David (2006) recently replicated by Nair, Palmer, Aleman, and David (2014), demonstrated that, generally, reduced executive function was correlated with lack of insight (i.e. worse executive function is related to worse insight). More specifically, scores on the Wisconsin Card Sorting Task (WCST) were also positively correlated with insight (i.e. more errors are related to worse insight), however this correlation was much smaller in the updated analysis by Nair (r=0.14) compared to the previous analysis by Aleman (r=0.23), which may be explained by a larger sample size in the most recent analysis. Nevertheless, the presence of a significant relationship between poor insight and mental flexibility (as measured by set shifting ability) provides support for the neuropsychological theory of insight in psychosis (Cooke et al., 2005; David, 1990) that proposes poor insight is, in part, the product of deficits in neurocognition.

3.1.2.3 Relationship with brain structure and function

In addition to cognitive and psychopathological correlates, recent research has focused on potential neural correlates of insight. Early studies suggested a relationship between poor illness awareness and increased ventricular volume (Takai, Uematsu, Ueki, & Sone, 1992), and reduced brain and intracranial volume (Flashman, McAllister, Andreasen, & Saykin, 2000). A theory gaining more support is that of the relationship between poor insight and reduced frontal lobe structure (Larøi et al., 2000; Morgan et al., 2010; Sapara et al., 2007; Shad, Muddasani, Prasad, Sweeney, & Keshavan, 2004; Spalletta, Piras, Piras, Caltagirone, & Orfei, 2014). However some studies identified no brain regions to be associated with insight (Bassitt, Neto, de Castro, & Busatto, 2007; David et al., 1995; Rossell, Coakes, Shapleske, Woodruff, & David, 2003). This may be due to the different methods employed to measure insight and analyse brain images. Nonetheless, the frontal lobe theory of reduced insight appears to have the greatest amount of support versus theories highlighting other brain areas.

A recent review by (David et al., 2012) demonstrated that areas of the Cortical Midline System (CMS) have consistently been associated, in structural and functional imaging studies, with insight. Further, Ouzir & Azorin (2014) identified a number of studies reporting that poor insight is related to hemispheric asymmetry, whereby the majority of related brain abnormalities are associated with the right hemisphere. In addition, it has been suggested that it is possible to link each insight dimension to certain brain structures (Shad, Muddasani, & Keshavan, 2006) where deficits in the dorsolateral prefrontal cortex (DLPFC) may result in illness unawareness by interfering with self-monitoring, while occipital frontal cortex (OFC) abnormalities may be related or mediate symptom misattribution. Further, reduced fractional anisotropy (FA; white matter connections) in the left middle and right superior frontal gyri, as well as the right and left cingulate gyri, was significantly associated with poor insight into illness (Antonius et al., 2011). Indirect support for this has also come from an open label transcranial direct current stimulation (tDCS) study, where patients with schizophrenia experiencing persistent auditory hallucinations received anodal stimulation of left DLPFC and cathodal stimulation over left temporo-parietal junction. Following tDCS, there was a significant improvement in illness awareness, as well as a significant reduction in auditory hallucination severity (Bose et al., 2014).

The general notion of impaired self-awareness has also been extensively researched in psychiatric populations. A review and meta-analysis by van der Meer et al. (2010) investigating the neural correlates of self-reflection in schizophrenia demonstrated that they are also related to the Cortical Midline Structures (CMS) as measured using PET and fMRI. Patients with damage to the CMS are often impaired in evaluating problems they face and often overestimate their capacities and performance. After close reading of the literature it appeared that, within the medial prefrontal cortex (MPFC), activation of the ventral MPFC (vMPFC) was related to processing of self-relevant information, whereas the activity within dorsal MPFC (dMPFC) was related to evaluation and decision-making processes regarding both self- and other-referential processing. It was theorized that, as good insight into illness requires intact self-referential processing, CMS integrity might also be related to illness awareness in patients with psychosis and schizophrenia. This relationship has since been supported using fMRI by Raij, Riekki, and Hari (2012), who measured activation in various brain regions whilst patients rated statements that were based on well-established insight assessments, such as “If someone said I have a mental illness they would be right.” It was found that patients’ insight was strongly correlated with increased activation in the CMS, where more activation was associated with better insight.

These findings indicate that similar areas of the medial frontal lobes are associated with both insight into illness and healthy adult introspection, suggesting that these neural regions make up the neural basis of metacognitive processes (Fleming & Dolan, 2012).

3.1.2.4 *TRAINING*

It has been suggested that cognitive and behavioural training could help improve insight into illness in patients. A meta-analysis by Pijnenborg, van Donkersgoed, David, and Aleman (2013) assessed the effect various forms of intervention can have on insight. Overall, analysis of 19 randomised control trial (RCTs) studies found that there was a significant moderate overall effect of treatments that measured the change in insight in psychotic disorders. However most studies measured insight as a secondary outcome, and thus more studies need to be carried out investigating the effect of an intervention specifically targeting insight. A sub-analysis of different intervention types was also carried out on CBT, psycho-education and adherence therapy studies; while no effect sizes reached significance (possibly due to lack of power) the effect size for CBT increased when CBT vs. treatment as usual studies were included.

Another recent review by McCormack, Tierney, Brennan, Lawlor, & Clarke, (2014) found results regarding the effectiveness of CBT on insight were conflicting. The authors suggest that this may be the result of differering theories of insight influencing the various treatments and the psychoeducational channels through which they are disemminated. Further limitations were identifed such as the variety of assessments employed across the studies reviewed which possibly correlated differently with individual aspects and outcomes of the CBT interventions.

Recently results of an RCT designed to improve insight (REFLEX; Pijnenborg et al., 2014) have indicated that a metacognitive training program improved clinical insight after a course of therapy. Further, evidence suggests that by using targeted psychotherapy, self-awareness of mental illness can be improved. Briki et al. (2014) have developed "Metacognitive training" (MCT), an 8-week group intervention therapy designed to improve self-reflection on cognitive biases and problem solving in patients with schizophrenia. Results indicated that there was only a trend improvement in insight scores, which they attribute to relatively high insight scores at baseline. A pilot investigation carried out 3 years earlier indicated that there was significant improvement on awareness scores in a group of patients who had lower baseline insight (Favrod et al., 2011).

One concern which has been raised when considering interventions aimed at improving insight is the effect they may have on mood (Cavelti et al, 2012), as there is a small but robust relationship associated with improved insight and depression severity (Mintz et al., 2003). Whilst the meta-analysis by Pijnenborg et al. (2013) states there were few reported effects on mood in association with improved insight, they note that this effect (following intervention) was rarely measured.

3.1.3 Clinical insight in Dementia

3.1.3.1 Relationship with psychopathology

A review by Aalten, Van Valen, Clare, Kenny, and Verhey (2005) found an association between insight and a number of clinical symptoms. The largest body of evidence suggests that insight in dementia is related to reported levels of depression, where better illness awareness is associated with lower mood (Mograbi & Morris, 2014; Marková, 2005). However some studies have indicated that only mild depression and dysthymia, as opposed to major depression, are related to level of insight (Migliorelli et al., 1995; Starkstein et al., 1997), and thus it may be that mild depression is manifested as depressive realism, whereas major depression results in less accurate appraisals due to more severe mood changes and increased feelings of hopelessness leading to negative self-appraisal. Further, some work has indicated that mania and pathological laughing are associated with worse awareness (Migliorelli et al., 1995). This lack of consistent evidence on this link between awareness and mood may be due to methodological limitations around measurement across studies, which may affect the apparent strength and degree of the relationship with each other (Aalten et al., 2005). It may also be the case that only specific dimensions of depression are associated with aspects of illness awareness (Mograbi & Morris, 2014), and thus studies that use more global assessments will miss these associations.

There is also some evidence to suggest that insight becomes worse as dementia progresses (Onor, Trevisiol, Negro, & Aguglia, 2006) and depression rates fall (Feher, Mahurin, Inbody, Crook, & Pirozzolo, 1991; Starkstein et al., 1997). There is therefore a suggestion that the presence of mild depression or dysthymia is a 'healthy' psychological reaction to perceived loss of abilities, such as memory or other cognitive faculties (Starkstein et al., 1997). Additional evidence suggests that as dementia severity progresses, awareness is reduced and mood improves (Wragg & Jeste, 1989). However, it has been found that, when awareness is split into domains, there is a correlation between only low mood and awareness of memory deficits, and not awareness of behavioural deficits (Chen et al., 2014). Hence, depression may occur early on in the condition when there is relatively good awareness but that as the disease progresses patients may even lose awareness of their affective symptoms; note that Verhülsdonk, Quack, Höft, Lange-Asschenfeldt, and Supprian (2013) identified large discrepancies between patient and caregiver ratings of patient depressive symptoms.

There is a small amount of evidence to suggest that apathy is also related to poor awareness of illness in dementia patients (Aalten et al., 2005; Mograbi & Morris, 2014) with SPECT imaging indicating that both apathy and lack of awareness of illness are both related to dysfunction in the right hemisphere (Ott, Noto, & Fogel, 1995). Anxiety has also been linked to higher levels of awareness (Aalten et al., 2005). In addition, delusional psychotic symptoms are have also been associated with poor awareness, however both lack of awareness and psychotic symptoms in dementia are related to dysfunction in the right frontal lobe, and as such this relationship may be related to a common neurological change as opposed to a direct correlation (Aalten et al., 2005).

There is also evidence for a link between age of onset and insight, where late onset-dementia patients are twice as likely to have poor insight compared to early onset patients (van Vliet et al., 2013). It is suggested that the higher number of functional demands on younger onset patients may expose them to more of their deficits, and thus make them aware. It may also be associated with underlying neuropathology, as younger onset patients show increased atrophy in posterior brain regions (van der Flier, Pijnenburg, Fox, & Scheltens, 2011), as opposed to areas in the medial temporal lobe that are known to be associated with awareness (see section 3.1.3.3).

3.1.3.2 Relationship with neuro-cognition

In addition to psychopathology, neurocognitive functioning is suggested to be a correlate of awareness of illness in dementia. Chen et al. (2014) found that lower scores on the Mini Mental State Examination (MMSE) were significantly associated with unawareness of both memory and behavioural deficits, and a number of studies have found an association between improved awareness and better executive function (Lopez, Becker, Somsak, Dew, and DeKosky, 1994; Michon, Deweer, Pillon, Agid, and Dubois, 1994). Zanetti et al. (1999) describe a “tri-linear” model of insight and cognitive ability as measured by the MMSE, whereby insight was consistently high for those with scores greater than 24 (MCI), and showed a steady decrease between scores of 23 and 13, and awareness was lowest for patients with an MMSE score lower than 12. One study has found that the relationship between poor insight and impaired cognitive function (mental control, visual perception and verbal memory) was only present when controlling for depressive symptoms (Smith, Henderson, McCleary, Murdock, & Buckwalter, 2000).

There is some evidence to suggest that people with MCI- which is frequently the prodromal phase of dementia- are actually more likely to overestimate their cognitive impairments, such as memory, when relating it to every day functioning, as opposed to patients with more severe impairments such as AD underestimating their deficits (Roberts, Clare, & Woods, 2009). Orfei et al. (2010) found that poor verbal memory performance was related to poor awareness in MCI patients. However there was no relationship between the two in AD patients, suggesting factors other than memory ability are related to awareness as dementia progresses.

A multi-dimensional analysis of 101 patients with dementia (Clare et al., 2011) found that reduced explicit awareness was related to age, lower MMSE scores and poorer memory function. It has also been reported that better awareness is related to better outcomes of cognitive training (Clare, Wilson, Carter, Roth, & Hodges, 2004).

There has also been research into experimentally controlled measures of awareness of memory and cognitive abilities found in the metacognition literature relating to MCI and AD patients, which was discussed in Chapter 2.

3.1.3.3 Relationship with brain structure and function

Lack of awareness in dementia has often been associated with lesions in the right parietal lobe and bilateral frontal lobes (Stuss & Benson, 1986), and a review by (Zamboni & Wilcock, 2011) identified that, though there was a large range of areas identified within the 18 studies analysed, findings were mainly located in the frontal and temporo-parietal regions.

Regarding functional correlates, Vogel, Hasselbalch, Gade, Ziebell, and Waldemar (2005) found that there was a relationship between discrepancy scores on a clinical memory questionnaire and activation in the right inferior frontal gyrus in a group of MCI and AD patients (as measured using regional cerebral blood flow). This relationship was also specific to self-awareness, as demonstrated by Zamboni et al. (2013), who found differences in brain activation in medial prefrontal and anterior temporal regions during self- and other-ratings in AD patients. Additionally, Sultzer et al. (2013) carried out a PET study and found low cortical metabolic activity in bilateral medial frontal cortex to be associated with poor insight.

A recent review by (Cosentino, 2014) also suggests that a specific reduction in the functional connectivity between cortical midline structures (CMS) affects awareness of cognitive deficits in dementia; namely the medial prefrontal cortex (mPFC) and anterior cingulate cortex (ACC; Ries et al., 2012) as measured on a memory rating discrepancy scale. Performance on a self-appraisal task (rating trait adjectives as self-relevant or not) has also been associated with activation in the MPFC and posterior cingulate cortex (PCC; Ries et al., 2007). Both structures appear to be functionally associated with accurate self-appraisal in healthy adults, and the ACC is involved in detection and response to errors, as well as monitoring conflict.

Recent evidence has also suggested that brain structure may be predictive of future conversion from MCI to AD. Spalletta et al. (2014) followed up patients with a first diagnosis of MCI for 5 years. They found that self-awareness and baseline structural MRI differed between those who were identified as converters at 5 year follow-up (converted from MCI to AD) compared to non-converters (did not convert to AD). Converter patients demonstrated worse awareness at baseline and their memory deficit awareness was associated with reduced gray matter volume in the ACC and the right inferior frontal cortex, and total awareness was associated with the cerebellar vermis. Non-converter patients, however, had better awareness at baseline and this was associated with reduced gray matter volume in the left superior and middle temporal areas, indicating that MCI and AD deficits are mediated by different mechanisms.

As stated in section 3.1.2.3, the same areas in the frontal lobes and CMS are associated with healthy adult introspection, adding further support to the suggestion that these neural regions make up the neural basis of metacognitive processes (Fleming & Dolan, 2012).

3.1.3 Clinical insight across diagnoses

The literature regarding awareness of illness tends to be split by diagnosis, however Gilleen, Greenwood & David (2009) compared awareness of patients with schizophrenia, dementia and traumatic brain injury (TBI), as measured using the standardised measures of awareness (Patient Competency Rating Scale [PCRS], the Scale to Assess Unawareness of Mental Disorder [SUMD], Dysexecutive Questionnaire [DEX] and Schedule for the Assessment of Insight [SAI]), in order to search for similarities and differences between the three clinical groups, and identify common mechanisms that mediate awareness. Though there are clear limitations regarding large age differences between the groups, all were comparable on premorbid IQ score. Results suggested that patients with dementia and TBI were much less accurate in appraisal of behavioural symptoms than those with schizophrenia. Additionally, the behavioural insight scores were not correlated with clinical insight scores (SAI and SUMD) in schizophrenia patients, as compared to a significant correlation in the whole group analysis. It was therefore suggested that behavioural awareness remains intact for schizophrenia, as opposed to organic disorders such as dementia and TBI, and this may be because the different domains of awareness are partially regulated by different processes. Further work by Gilleen, Greenwood & David (2014) has demonstrated that there was a greater association between memory awareness and memory function itself than between memory and awareness of illness in patients with dementia.

3.1.5 Clinical insight conclusions

There are clear and similar disturbances in illness self-awareness in patients with FEP, schizophrenia and dementia, where both severity of symptoms and cognitive function are significantly related to insight. There is also structural and functional neuroimaging evidence for a neurological component of insight, mainly located, but not limited to, the medial frontal lobes. These neurological bases of "self-concept" also appear to be modular, with specific areas related to specific processes such as understanding, awareness or processing information about the self. Further, recent evidence suggests that there may be some difference between the profiles of self-awareness for behavioural function across diagnosis (Gilleen, Greenwood & David, 2009).

3.2 Cognitive insight

A complementary addition to the concept of clinical insight was introduced by Beck et al. (2004), named "cognitive insight", which focuses on the "thinking style" biases associated with unawareness of illness, rather than those due to information processing efficiency, that are often present in patients with psychosis. More specifically, cognitive insight can be defined as a patient's ability to self-reflect and also the level of self-certainty they feel in the interpretation they give to their unusual (illness-related) experiences. Though an idea conceived in the clinical field of self-awareness research, cognitive insight is similar concept to "attributive metacognition" (David et al., 2012), which was initially investigated in the psychological literature (Saxe & Offen, 2010).

Cognitive insight addresses four key impairments characterised by patients with a lack of illness awareness: impairment in the ability to be objective when considering delusional experiences and cognitive distortions, a reduced capability to put such experiences into perspective, unresponsiveness to corrective information from others and an overconfidence in conclusions regarding delusional judgments. Therefore, whilst clinical insight assesses patients' understanding that symptoms are a manifestation of mental illness and require treatment, cognitive insight seeks to understand the metacognitive processes involved in how those judgements are made and maintained.

3.2.1 *MEASURING COGNITIVE INSIGHT*

Beck at al. (2004) developed the Beck Cognitive Insight Scale (BCIS) to measure patients' ability to distance themselves from and re-evaluate unusual beliefs and misinterpretations of situations and perceptions. The BCIS is a 15 item self-rated questionnaire, where each item requires a response on a 4 level scale; 1. Do not agree at all, 2. Agree slightly, 3. Agree a lot, 4. Agree completely. The items can be separated into 2 sub-scales, 9-item self-reflection (SR: "ability to reflect on whether their thoughts and beliefs about him or herself are correct, or could be changed by someone else's opinion") and 6-item self-certainty (SC: "degree of overconfidence people have in their interpretations of their experiences"). A composite index can be calculated by subtracting SC from SR (see chapter 5.4.4 for a more detailed description of the scale).

A recent review of the literature and the scale itself (Riggs, Grant, Perivoliotis, & Beck, 2012) states that seven studies have confirmed the 2-factor structure of the BCIS suggested by Beck et al. (2004) for inpatients, and this structure has been replicated in outpatients, first-episode psychosis patients, as well as healthy controls using numerous factor analysis methods. Riggs et al. also report that the internal consistency of the scale is sound, with all but one study demonstrating the SR subscale produced a Chronbach's alpha score of greater than or equal to .7, and all but 2 studies showed internal consistency for the SC subscale to be greater than or equal to .7. Additionally three studies demonstrated that the scale has good test-retest reliability in both patients and healthy controls. One recent study of 120 patients (Merlin et al., 2012) identified a 4-factor structure, self-certainty, self-reflectiveness, openness to external feedback and infallibility of self-reflection, and asks whether a 4-factor structure may help identify the further intricacies of cognitive insight. Though this study used the Tamil version of the BCIS (BCIS-T), the researchers used back translation, and thus this measure is considered to be comparable to the original BCIS. That said, subtle cultural differences in the meaning of the questions in the additional two factors might explain the differences in factor structure.

As noted, the BCIS has shown good test-retest reliability (Uchida et al., 2009), however there are few data on whether cognitive insight can improve over time. A recent metacognitive training intervention RCT aimed at improving insight in psychosis patients, the REFLEX study (Pijnenborg et al., 2014), found that whilst clinical insight improved after an 8 week course of a behavioural intervention, cognitive insight remained unchanged. This lack of change in cognitive insight could be explained as follows; as patients began to understand more about their illness throughout the course of therapy, statements from the BCIS which are thought to indicate an overconfident bias in the way patients think (e.g. “My interpretations of my experiences are definitely right”, and “I know better than anyone else what my problems are”) take on a different meaning and actually reflect better self-understanding after the course of therapy. The difficulties in interpreting certain BCIS items below will be covered further below.

The BCIS has been shown by most studies to distinguish between psychotic and nonpsychotic patient groups using the CI sub-scale, where patients experiencing psychosis score significantly lower than non-psychotic patients (Bora, Erkan, Kayahan, & Veznedaroglu, 2007). However there is still some debate as to whether this is the case with bipolar patients (Colis, Steer, & Beck, 2006) and depressed patients given the work of (Mass, Wolf, & Lincoln, 2012), who found equal BCIS scores in schizophrenia and mixed (mostly unipolar depressed) patients.

In addition to the original aims of developing the BCIS regarding illness awareness, the scale has also been demonstrated as suitable for use in community and healthy population samples (Buchy, Brodeur & Lepage, 2012), which have produced the same 2 factor structure of the BCIS as patient populations in a factor analysis. This has also been demonstrated in other, selected, non-clinical populations (Uchida et al., 2009). However this calls in to question what happens when healthy adults do not have, or are unable to relate to the term, "unusual experiences", akin to those noted in clinical populations. Further, it has been said that one needs to have 'something to have insight about' before it can be measured (Marková, 2005). In the case of the BCIS, the nature of most questions deem it suitable for use in the healthy population, but what is being assessed in healthy adults is not the same 'something' as in patients. While high self-certainty and low self-reflection may result in distorted self-belief and poor correction of this in patients, it could reflect a realistic grasp of facts and events in healthy adults.

All in all, the results suggest that the BCIS is a valid instrument to assess cognitive insight in the general population, but it should be noted that what is being measured may be subtly different in patients and healthy volunteers.

With this is mind, it is also important to note that BCIS subscales have shown a variable ability to distinguish between patients with psychosis and healthy controls. A number of studies have demonstrated that patients could be identified as having a significantly lower CI score (Beck et al., 2004; Colis et al., 2006; Martin, Warman, & Lysaker, 2010), however there is no absolute cut off score to discriminate between healthy individuals and patients. Additionally, while patients have been identified as scoring significantly higher on SC sub-scale (Martin et al., 2010), there is still some debate as to whether controls and non-psychotic patients score significantly higher on the SR subscale compared to psychotic individuals. One large scale study reported a significant difference between groups where controls score significantly higher on the SR subscale (Bora et al., 2007; n=93 FEP, 43= non FEP), while there are two studies reporting no significant difference between psychotic and non-psychotic psychiatric patients (Colis et al., 2006 [major depressive disorder n=56; paranoid schizophrenia and schizoaffective disorder n=42; bipolar i disorder n=52; bipolar I with manic episode n=18; bipolar I with mixed or depressive episode n=34]) as well as psychiatric patients and controls (Engh et al., 2007 [schizophrenia n=143; bipolar disorder n=92; controls n=64]). Thus the BCIS may be a useful tool to measure the difference in self-awareness of healthy controls and patients, as well as between patient groups, but results should be interpreted with caution.

3.2.2 RELATIONSHIP WITH PSYCHOPATHOLOGY

A positive relationship has been consistently reported between delusion severity and SC (Engh et al., 2010; Ouzir, Azorin, Adida, Boussaoud, & Battas, 2012; Warman et al., 2007). The BCIS is also sensitive to delusion proneness in otherwise healthy individuals (Warman & Martin, 2006) with delusion-prone individuals scoring higher on the SC items than non-delusion prone participants. Interestingly, non-delusion prone patients also showed higher SR scores, and were more likely to acknowledge their other biases such as jumping to conclusions. The authors go on to suggest that it is a lack of self-reflection that may cause some, but not all delusion-prone individuals, to later make the transition into a psychotic disorder. Further, recent evidence has demonstrated that patients in an “at risk mental state” (ARMS: associated with a higher risk of transition into a psychotic episode) demonstrated a positive correlation between delusional thinking and SC scores, indicating that those with near psychotic-threshold delusional thinking had higher SC and thus more impaired cognitive insight (Uchida et al., 2014). This study also reported that ARMS patients scored significantly higher than healthy controls on the SC sub-scale. It could therefore be suggested that delusional thinking is related to cognitive insight because low SR and high SC, which produces a low BCIS-CI (composite index) score, result in a reasoning style that can maintain delusional beliefs. In essence, high self-certainty is associated with poor cognition and cognitive rigidity (Nair et al., 2014), and poor cognition is associated with poor decision-making and the avoidance of rational thinking (Bruine de Bruin, Parker, & Fischhoff, 2007;

Stanovich & West, 2008). It is suggested that one requires greater cognitive capacity to think about and reflect on potentially erroneous beliefs, whilst it requires less capacity to make a quick decision and stand by it (such as jumping to conclusion bias; Garety et al., 2013). Similarly, patients who demonstrate increased SR and reduced SC are less cognitively rigid, are more open to alternative explanations for their experiences, and are predicted to be less delusion-prone.

In relation to positive symptoms, the majority of studies have reported a relationship between Positive and Negative Syndrome Scale scores (PANSS; Kay, Flszbein, & Opfer, 1987) and BCIS (Riggs et al., 2012), with a significant positive correlation between PANSS positive symptom score and SC, and a negative relationship with SR and CI (probably driven by the SR score; Mass et al., 2012; Mohanty & Kumar, 2012). In addition to differentiating between patients with delusions and healthy controls, both chronic and FEP patients with delusions have been reported to score lower on SR, with SC producing a non-significant trend towards higher scores and worse delusions.

The research into cognitive insight and negative symptoms has produced mixed results. Although it has been suggested that there is a logical link between negative symptoms (such as withdrawal or lack of function and flat affect) and cognitive insight (Riggs et al., 2012) there is scant evidence to suggest that reduced SR and increased SC are correlates of negative symptoms as measured on the PANSS, with an equal number of studies supporting and refuting the claim.

As noted in the previous section, low mood is significantly related to better clinical insight in a number of patient groups (Mintz, 2003); it has therefore been suggested that cognitive insight may also be linked to mood. Granholm et al. (2005) reasoned that patients who are able to understand and reflect on their unusual cognitive experiences, and subsequently gain both cognitive and clinical insight, might also become more depressed as they lose confidence in their previous incorrect beliefs and understand their experiences were symptoms of their illnesses. Hence, if an increased ability to self-reflect about one's experiences and problems leads to depression, one might expect a close relationship between SR and mood. Alternatively, if low mood leads to depressive realism (Ackermann & DeRubeis, 1991; Haaga & Beck, 1995) or less self-serving bias (blaming external factors for one's misfortune), this may mean that there is less need for self-reflection to correct such a bias. In this way, one could speculate that strong links between self-reflection and mood would better support the notion that changes in awareness follow changes in mood.

The supporting evidence for the association with mood, for whatever reason, appears mixed. The initial paper presenting the BCIS by Beck, Baruch, Balter, Steer, and Warman (2004) demonstrated that there was no correlation in psychosis patients' depression scores and any BCIS sub scale, however they did report a significant correlation between patients with Major Depressive Disorder and SR. The lack of association between mood and BCIS in psychosis was replicated by Pedrelli et al., (2004), whose sample consisted of adult men over the age of 40 and used a different measure of depression. However, since these initial studies Beck and colleagues have found results in the opposite direction (Riggs et al., 2012), with SR showing a trend in the literature towards a significant relationship with mood. A total of 15 studies have reported correlations between BCIS scores and depression; 11 have reported a positive relationship between SR and worse mood (Beck et al., 2004; Colis, Steer, & Beck, 2006; Ekinci, Ugurlu, Albayrak, Arslan, & Caykoylu, 2012; Greenberger & Serper, 2010; Kao, Wang, Lu, & Liu, 2011; Mass, Wolf, & Lincoln, 2012; Misdrahi, Denard, Swendsen, Jaussent, & Courtet, 2014; Raffard et al., 2013; Tastet, Verdoux, Bergua, Destaillats, & Prouteau, 2012; Warman, Lysaker, & Martin, 2007; Wiffen, 2011) 1 with no discernible effect (Gilleen, Greenwood, & David, 2011) and 2 small negative, non-significant correlations (Granholm et al., 2005; Pedrelli et al., 2004).

A similar relationship has also been reported between anxiety and SR scores, with most studies reporting positive relationships between worse anxiety symptoms and both SR and CI, with one study reporting no effect (Riggs et al., 2012). Again, this relationship may be related to the rumination symptoms present in anxiety, which may be seen as a form of continued self-reflection. Therefore the evidence that mood and BCIS are related through a self-reflection pathway is compelling (see chapter 6 for meta-analysis of BCIS and mood), however the basis for the association and direction of causality has not yet been established.

A recent study by Giusti et al. (2014) investigated the relationship between cognitive insight and perceived recovery (using the Recovery Assessment Scale [RAS; Corrigan et al., 1999, 2004]), reporting a negative association between scores on the RAS and BCIS-SR, however RAS scores were positively associated with severity of psychopathology. A multiple regression model demonstrated that lower clinical insight, higher neurocognitive abilities and lower social functioning were the significant predictors of personal recovery. Results therefore demonstrate that better perception of recovery by the patient was actually correlated to a lower ability of patients to self-reflect. The authors describe recovery as a subjective experience as well as an objective remission of symptoms, and thus indicate that, whilst cognitive insight is associated with symptoms, it is not associated with personal interpretation of illness and recovery in patients with schizophrenia.

A longitudinal study has also indicated that cognitive insight scores are good predictors of social functioning at 1 year follow up (O'Connor et al., 2013) as measured by the Global Assessment of Functioning (GAF). This has not been reported often in other studies, and the authors suggest that this is because GAF scores are more general than measures such as the PANSS which measures specific symptoms separately, and thus the relationship between cognitive insight and depression or delusions may have been the driving force behind this significant association.

3.2.3 Relationship with clinical insight

Riggs et al. (2012) report that convergent validity of the 'cognitive insight' construct has been determined by looking at the association between the BCIS and 5 different measures of clinical insight. Beck, along with two other research groups, has demonstrated that cognitive insight is a significant predictor of illness awareness as measured on the Scale to Assess Unawareness of Mental Disorder (SUMD; Amador et al., 1993) with moderate-to-large correlations between cognitive insight and the awareness of a mental illness item (Lepage et al., 2008) and the total score (Bora et al., 2007).

The relationship between BCIS score and other measures of clinical insight, such as PANSS, Birchwood Insight Scale (BIS) and Schedule for the Assessment of Insight (SAI) is weaker, with mild to moderate correlations reported for each (Riggs et al., 2012). This may be because cognitive and clinical insight measures are looking at subtly different psychological constructs. Again, looking at the REFLEX trial, a significant improvement in clinical, but not cognitive, insight was found after a course of metacognitive remediation therapy (Pijnenborg et al., 2014) emphasizing the difference between the two measures. Further evidence for a conceptual difference between the two forms of insight is the finding reported previously that cognitive insight, not clinical insight, is a good baseline predictor of social function at 1-year follow-up (O'Connor et al., 2013).

3.2.4 Relationship with gender

There has been little research into the effect of gender on cognitive insight (Martin et al., 2010), partly because there are often significantly more men in clinical psychosis samples, and women in control samples. The original paper by Beck et al., (2004), reports no gender effect. Though Warman et al., (2007) reported a gender effect when comparing scores of patients and healthy adults, it was suggested that this was due to the majority of women being in the healthy control group and was thus an artefact. This may explain the lack of gender effects in the previous literature.

Kao et al. (2013) investigated the potential effect of gender on cognitive insight, in relation to executive function. Their results demonstrated, using logistic regression, that poor cognitive insight was significantly related to impaired executive function and was mediated by gender, wherein poor executive function was significantly correlated with impaired cognitive insight for males with schizophrenia, but not for females, based on the SR sub-scale.

3.2.5 *Relationship with neuro-cognition*

Given that clinical insight is partly associated to neurocognitive functioning, it follows that cognitive insight should also demonstrate links, given it is related to cognitive processing of illness related information. Findings in this area, however, have been mixed. A recent preliminary meta-analysis by Nair et al. (2014) investigated the relationship between cognitive insight and total cognition, memory, executive function. This analysis revealed that BCIS sub-scales differ in terms of their relationship to neurocognitive functions. More specifically, the composite index was significantly associated with “total cognition” and memory, driven by the SC scale, whereas SR was not significantly correlated with any measure of neurocognition.

3.2.6 *Relationship with brain structure and function*

A great deal of research into self-reflection as a more general concept has been reported in the healthy metacognitive (chapter 2.3.2) and clinical (chapter 2.4.1.2 and 3.1.3.3) literature. Therefore, this section will focus on the neural correlates specific to the BCIS sub-scales.

A recent MRI study by Orfei, Piras, Macci, Caltagirone, and Spalletta (2013) found that, in 45 outpatients with schizophrenia and 45 age- and gender-matched healthy controls, there was a positive correlation between SR and gray matter volume in the right ventro-lateral prefrontal cortex (VLPFC), an area that is thought to be crucial for working memory when creating and maintaining different hypotheses about the self. There were no significant neural correlates of SC. Additionally, there was no correlation between BCIS scores and white matter connectivity, as identified by diffusion tensor imaging (DTI).

Another recent study by Pu et al. (2013) investigated pre-frontal function in cognitive insight and during a cognitive task using near-infrared spectroscopy (NIRS) procedure (a functional neuroimaging technique). They studied 30 patients with clinically stable schizophrenia and 30 age- and gender-matched healthy controls. Their results implicated reduced functioning in the prefrontal and temporal regions of the brain in patients, as characterised by reduced hemodynamic changes during multi-channel NIRS. There was a significant positive relationship between SR and the right ventrolateral prefrontal and right temporal functions during a verbal fluency task (measure of executive function). Results suggest that activity in the right VLPFC and temporal cortical regions was associated with cognitive insight in patients with schizophrenia.

Similarly, Buchy et al. (2014) investigated the relationship between external source memory, as measured using a virtual reality landscape during fMRI, and activation of the frontal cortex including VLPFC, temporal and occipital cortices. A significant relationship was identified between VLPFC activity and higher SR scores, with significant associations between the midbrain and lower SC scores during source memory attributions. However no significant relationship was found between either measure of cognitive insight and source memory accuracy.

Evidence from brain imaging studies confirms that there are similar brain regions associated with both BCIS SR and attributive metacognition, the temporal parietal junction and the MPFC (Saxe & Offen, 2010), further supporting the notion that the two concepts are related on a neural basis.

3.2.7 *Cognitive insight - conclusions*

Overall it appears that there is some measurable relationship between cognitive insight and psychopathology; a stronger relationship with positive symptoms and worse cognitive insight, driven by the SC subscale has been reported and there is evidence for a similar yet weaker relationship between SC and negative symptoms. There is also a growing body of evidence to suggest a link between low mood and better cognitive insight, driven by the SR subscale. There is also evidence to confirm a moderate but significant relationship between clinical and cognitive insight, implying that they are separable but associated concepts. There is equal support for a small but significant relationship between neurocognitive functioning and cognitive insight, specifically SC and both total cognition and memory. As in clinical insight, initial investigations into the structural and functional correlates of cognitive insight have implicated areas in the frontal lobe relating to SR, and midbrain structures relating to SC. Further, these associations indicate a similar neural basis for SR and attributive metacognition.

The BCIS may be suitable for use with healthy adults, and therefore also for comparisons between healthy and clinical populations. As there are few clinically relevant assessments designed for use with clinical groups that are also suitable for use in the healthy population, this measure may be important for teasing out deficits of self-appraisal in a variety of neuropsychiatric patients. All in all, this growing body of work suggests that the concept of cognitive insight has some utility in the field of insight research, with the potential for clinical applications.

3.3 Measures of clinical insight

There are a number of methods used to assess self-awareness and clinical insight in psychiatric conditions, usually developed for a specific disorder. Such methods can be 1) self-rated by patients, 2) utilise ratings from a significant other or clinician, or 3) use discrepancy measures where rating 1) is subtracted from rating 2).

3.3.1 *Developed for Schizophrenia*

See table 3.3-1 for correlations between measures of insight developed for schizophrenia patients.

	Scale A	Scale B	Schedule for the Assessment of Insight (SAI)	SAI-Extended (SAI-E)	Positive and Negative Syndrome Scale (PANSS)	Insight and Treatment Attitudes Questionnaire (ITAQ)
Scale A		0.239	0.44*	0.466**	0.544**	0.545**
Scale B	0.229		0.336	0.410*	0.423*	0.411*
SAI	0.400*	0.336		0.977***	0.823***	0.823***
SAI-E	0.466**	0.401*	0.977***		0.895***	0.845***
PANSS	0.544**	0.423*	0.884***	0.895***		0.904***
(ITAQ)	0.545**	0.411	0.845***	0.845***	0.904***	

Table 3.3-1 Shows correlation coefficients (Pearson's r) between insight scales developed for use with patients diagnosed with schizophrenia, adapted from (Sanz, Constable, Lopez-Ibor, Kemp, & David, 1998); * p<.05; **p<.01; ***p<.001.

3.3.1.1 *Self-report*

A commonly used self-report insight scale is the Birchwood Insight Scale (BIS; Birchwood et al., 1994). Based on the three-dimensional insight model (David, 1990) it has 11 items to assess patients' awareness in each domain. The scale has demonstrated good test-retest reliability, and is also correlated with a clinician rated insight scale (Young, Campbell, Zakzanis, & Weinstein, 2003), the Scale to Assess Unawareness of Mental Disorder (SUMD; Amador et al., 1993). However, Young et al. also found that patients scored significantly lower on the BIS than the SUMD regardless of which assessment was administered first.

Marková and Berrios (1992) devised a scale based on the premise that "individuals hold views not only about the disorder affecting them but also about how the disorder affects their interaction with the world". It is made up of 32 "yes/no" questions, which relate to self-perception of illness related statements. The items are split into two sub-scales, where a positive answer indicates greater insight (Scale A), and items where a positive response indicates less insight (Scale B). This scale can either be completed by the subject or by a clinician. Scale A appears to be more frequently, highly, positively correlated with other measures of insight, and not correlated with Scale B (see table 3.3-1).

3.3.1.2 *Clinician rated*

The most basic clinical measure of insight used with schizophrenia patients is the PANSS insight item (Kay, et al., 1987). This is part of a 30-item psychopathology scale that is rated using a semi-structured interview, and to use it, raters should have standardised training. The insight item asks the clinician to rate a patients' "Lack of judgment and insight" on a scale of 1-7, where a score of 1 relates to "no impairment" (i.e. patient doesn't show a lack of insight) and 7 relates to "severe" (i.e. patients shows a severe lack of insight). Despite being a single item, this scale shows a moderate to high, significant, positive correlation with other standard measures of insight (see table 3.3-1).

A more commonly used scale is the Insight and Treatment Attitudes Questionnaire (ITAQ; McEvoy et al., 1989). This scale uses a semi-structured interview, including items that measure recognition of mental disorder (5 items) and attitudes to medication, hospitalization and follow-up evaluation (6 items). Items are scored from 0 (no insight) to 2 (good insight). This scale shows moderate to high, significant, positive correlations with other commonly used insight scales (see table 3.3-1).

Another commonly used scale is the SUMD (Amador et al., 1993), which is based on a structured interview. Though this scale can be used for assessment of a number of disorders, it is primarily used in schizophrenia research. This scale is made up of general measures (6 items), which measure global awareness of mental disorder, awareness of the effects of medication and awareness of social consequences of having a mental disorder. There are an additional 4 sub scales (17 items each), which measure current awareness of symptoms, retrospective awareness, current attribution of symptoms, and retrospective attribution of symptoms. Each item is given a score between 1 (good awareness) and 5 (poor awareness). The different sections can be used independently of one another if necessary. In an initial assessment (Amador et al., 1993), it was reported that scores on the first 3 general items of the SUMD correlated positively with insight ratings on the Mental Status Examination and the insight rating on the Hamilton Depression scale. There was also a correlation between the SUMD total awareness scores and Mental Status Examination scores.

Another commonly used scale to assess insight is the Schedule for the Assessment of Insight (SAI; David, 1990) and the SAI-Extended (SAI-E; Kemp and David, 1997). This scale uses a semi-structured interview to rate awareness of illness, need for treatment and awareness of symptoms (9 items) as well as treatment compliance (3 items). Scores for the first 6 items (insight into illness and need for treatment) are between 0 (no insight) and 2 (good insight), 3 items regarding symptoms and reappraisal are scored from 0 (no awareness/bizarre explanation) to 4 (good insight/understanding). 3 items regarding medication compliance are rated using clinical notes or patients' primary carer in a separate scale (A-C). Both the SAI and the SAI-E scores are highly, positively correlated with ITAQ, PANSS and Scale A, whilst SAI-E is also highly correlated with Scale B (see table 3.3-1). The SAI-E total is also highly correlated with the SUMD total ($r=.84$, $p<.01$) and sub-scales (mental awareness, $r=-.82$, $p<.01$; medication, $r=-.81$, $p<.01$; awareness, $r=-.62$, $p<.01$; attribution, $r=-.86$, $p<.01$; Gilleen et al., 2010).

3.3.2 Developed for Dementia

A review by Clare, Marková, Verhey, and Kenny (2005) reports on and critically appraises the main approaches to assessing awareness in patients with dementia. The main methods identified were 1) clinician ratings of awareness, 2) calculation of discrepancies between carers' ratings and patients' self-ratings 3) calculation of an awareness score based on the discrepancy between patients' self- ratings and their performance on specific tasks (similar to those described in Chapter 2) and 4) a combination of the above methods.

3.3.2.1 *Clinician/Informant ratings*

As in schizophrenia research, a popular method of assessing awareness of patients with dementia is using clinical or researcher ratings, taken from semi-structured interviews or clinical notes. The most basic form of this assessment is the insight item of the Clinical Dementia Rating scale (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982), a scale designed to assess patients' awareness of memory impairment, where the final item allows the clinician or researcher to make a judgement regarding patients' "assessment of disability and station in life and understanding of why he/she is present at the examination*"*. Scores range from 0 (little insight) to 2 (full insight).

The SUMD (section 3.6.1.2) was designed for use with a number of neurological disorders and is therefore also suitable for use in the dementia population.

3.3.2.2 *Discrepancy scores*

Discrepancy scores are often used to assess a patients' awareness of their memory and behavioural deficits. To calculate, patient ratings of their abilities are subtracted from the informant ratings; positive scores indicate patients are underestimating their disability and negative scores indicate patients are over-estimating their disabilities. These measures often deem the patients' caregiver or informant to be an objective gold standard, which is not necessarily the case as they may be biased towards a higher or lower impairment rating depending on their mood or perceived quality of life (Clare, 2004a; 2004b). However, despite the potential risk of bias, they have consistently shown patients tend to underestimate their cognitive and behavioural deficits compared to the assessments of caregivers (David et al., 2012).

One commonly used assessment is the Dysexecutive questionnaire (DEX; Burgess, Alderman, Evans, Emslie, & Wilson, 1998), a sub-test of the Behavioural Assessment of the Dysexecutive Syndrome (BADS), which assesses patients' awareness of their behavioural and executive function. Patients and their caregivers complete a 20-item questionnaire that asks them to rate the frequency with which the patient displays certain behaviours in everyday life (see Chapter 5 section 5.4.3 for full description). A discrepancy score is calculated by subtracting patients' ratings from their care-givers' ratings. This scale is suitable for use within the general population as it is asking users to rate their executive and behavioural abilities rather than disorder-specific symptoms.

3.3.2.3 Task performance discrepancy scores

Task-performance discrepancy scores often come from tasks such as FOK and JOL, which have already been described in Chapter 2. These scores are more specific to types of memory function than clinical and practical outcomes.

3.3.2.4 Combination methods

It is believed that there may be some bias from carers and clinicians in typical discrepancy and clinician rated assessments, where carers may over- or under-evaluate a patients' behaviour and deficits, and similarly clinicians have limited exposure to the patient outside of clinical settings and therefore may not make accurate judgements. Ratings can also be subjective and vary according to the schedule used to obtain them. To address this issue, Clare et al. (2002) developed the Memory Awareness Rating Scale (MARS). The questions that form the items of the MARS are based on the Rivermead Behavioural Memory Test (RBMT; Wilson et al., 1985). The MARS allows clinicians and researchers to compare patients' memory ratings, task performance ratings and actual performance scores, as well as ratings of everyday situations. For some memory and behavioural scales, patients are required to rate how well they will do (prediction) and then how well they did (performance) on the task and how well other people of the same age would perform; ratings are made on a five-point scale ranging from better than average (0) to a lot worse than average (4), where a low score is related to good perceived performance. For other aspects of the scale carers are asked to rate how well a patient does everyday tasks. Discrepancy scores are calculated by subtracting patient response from carer or performance scores. As the tasks are related to everyday memory and behavioural experiences, as opposed to standard lab-based experiments, the MARS is therefore considered to be more ecologically valid that other discrepancy assessments.

The clinical methods described above can be referred to as "global" measures of awareness, and are related to general functioning in activities of everyday living, and can be useful when making clinical and practical decisions. Task specific discrepancy scores, as described in Chapter 2, are related to specific cognitive processes and allow a more detailed look into the specific processes that are disturbed in patients' awareness (Cosentino, 2014). It is therefore useful for researchers to use a combination of both when investigating the nature and effects of lack of insight in clinical patients so that a fuller picture can be gained from the information gathered.

3.3.2.5 Measures of Clinical Insight - Conclusions

Insight in neuropsychiatric disorders such as dementia and schizophrenia can be assessed using a number of measures, which are either rated by clinicians, carers or the patients themselves. Though many awareness scales used within these patient groups are correlated, there are a number of criticisms that can be made of each type of method, as discussed above. Plus the fact that there is evidence to suggest that patients demonstrate varied awareness depending on the situation they are in (Weinstein, Friedland, & Wagner, 1994) which could affect both clinician and carer ratings of patient awareness. Nevertheless, considerable progress has been made in developing practical, quantitative and reasonably reliable measures to assess awareness in clinical and experimental contexts.

3.3.3 Implicit Awareness

Finally it is worth noting that (Mograbi & Morris, 2013) detail evidence that, though outwardly appearing to have poor awareness of their functional problems, some patients with dementia and hemiplegia show an "implicit" awareness. Evidence to support this in patients with dementia comes from Martyr et al. (2011), who found that patients with dementia still showed an emotional Stroop effect for memory failure words, and Mograbi, Brown, Salas, and Morris (2012) who found that patients with dementia showed a normal emotional reaction in response to failure on tasks, indicating an unconscious awareness of their failure.

Though developed in the dementia literature, this has also been investigated in the psychosis literature. When carrying out a similar task to dementia patients, psychosis patients did not show any interference with psychosis-related words (e.g. crazy, schizophrenic) over and above words associated with physical disease (e.g. cancer; Wiffen et al., 2013). Further, there was a correlation between and explicit measure of illness awareness and interference on illness-related words, indicating that these words were less emotionally salient and appear to be less associated with the self in patients with poor insight. Together, these findings indicate that patients with psychosis have a genuine reduced awareness of their illness, as opposed to utilising a motivated denial mechanism where on some level they are aware that their experiences are illness related.

CHAPTER 4

4. AIMS AND HYPOTHESES

This project aimed to investigate the neurocognitive basis of metacognition and insight, including experiments with healthy volunteers and patients with psychosis and those with early stage dementia (ED). The four main aims were:

A. To investigate the effect of normal ageing on metacognitive tasks of perception and memory

B. To investigate the cognitive systems and mechanisms underlying metacognitive efficiency and patients' insight into illness, and discover whether the two are separate.

C. To investigate how current mood and presence of depression affects insight and metacognitive efficiency, and if this link is more evident in clinical populations compared to healthy controls.

D. To investigate whether deficits in metacognition and insight are caused by similar cognitive and neural systems across different diagnoses.

The following hypotheses were tested:

4.1 METACOGNITION IN THE HEALTHY POPULATION AND PATIENTS

$H^{4.1\text{-}1}$. There will be a negative association between metacognitive efficiency and age in both perceptual and memory domains. It is predicted that metacognitive efficiency (meta d'/d') will decline as participant age increases to a greater degree than would be predicted by age-related declines in performance alone, because under the ideal observer model meta d' is expected to be equal to d', therefore the decrease in meta d'/d' shows an impairment in metacognitive function above and beyond what is expected based on task performance.

$H^{4.1-2}$.There will be a positive correlation between the two domains of metacognitive efficiency. It is assumed that, despite differences in primary task performance according to type of task, ability to judge one's own performance on each task, and efficiency with which this judgement is performed, should be in part related to a common cognitive process.

$H^{4.1-3}$ There will be a positive correlation between executive function and metacognitive efficiency, in both domains. As metacognitive function in healthy adults has previously been associated with structure and function of the frontal lobe and executive function, it is predicted that better efficiency in our experimental measures of metacognition will be related to more optimal scores on standard tests of executive function (over and above IQ).

4.2 METACOGNITION AND MOOD

$H^{4.2}$.There will be a positive association between metacognitive efficiency and low mood as measured on the Beck Depression Inventory II (BDI), in both the perceptual and memory domain, akin to findings from qualitative measures of metacognitive function.

4.3 METACOGNITION AND AWARENESS

$H^{4.3}$ There will be a significant relationship between metacognitive efficiency and measures of awareness (Beck Cognitive Insight Scale, DEX and SAI-E) in both healthy controls and patients. It is assumed that, as more objective metacognitive judgements regarding task performance and awareness measures both rely on self-reflective processes, there will be a positive relationship between the two types of measure, where better awareness is associated with better metacognition.

4.4 METACOGNITION IN PSYCHIATRIC POPULATIONS

$H^{4.4}$. Patients experiencing their first episode of psychosis (FEP) or early-stage dementia (ED) will have lower metacognitive scores than healthy controls. As some patients with these disorders have poor awareness of illness it is also assumed that their general self-referential processing is also poor compared to healthy adults.

4.5 Insight in psychiatric populations

$H^{4.5\text{-}1}$ A meta-analysis investigating the relationship between mood and cognitive insight will demonstrate an overall positive association between self-reflection and depression, following qualitative evidence reported in a recent review.

$H^{4.5\text{-}2}$ There will be a significant correlation between measures of insight in psychiatric populations. There is robust evidence from previous research to suggest that there is an association between measures of awareness.

4.6 Neuroimaging

$H^{4.6\text{-}1}$ There will be a significant relationship between the volume of areas of the frontal lobe, such as the BA10, anterior cingulate cortex (ACC) and medial prefrontal cortex (MPFC), and metacognitive efficiency scores in patients with ED. Previous research in healthy adults has demonstrated there is a link between individual differences in metacognitive ability and the prefrontal cortex structure, and self-reflective processes in patients have been associated with structural imaging measures of the MPFC and the ACC.

CHAPTER 5

5. METHODS: PARTICIPANTS, BEHAVIOURAL ASSESSMENTS AND PROTOCOLS

5.1 RECRUITMENT

5.1.1 HEALTHY PARTICIPANTS

Three methods were employed to recruit healthy participants, so that a representative sample of the general population could be obtained. This aimed to ensure that results could be generalised to the wider healthy adult population as far as possible.

1. Some healthy control participants were recruited by approaching participants who had completed participation in an existing study at the Institute of Psychiatry; European Union Gene Environment Interaction (EU-GEI; PI Dr C Morgan). The study recruited a large sample of healthy participants from South London, in the boroughs of Lambeth and Southwark. Participants who had agreed to be re-contacted for further studies were approached by a phone call from the student in the first instance, explaining the study and asking if they were interested in taking part. Participants responding to the EU-GEI study invitation letter but who were unsuitable for the initial study due to quota sampling were also passed on to this study.
2. A copy of the Royal Mail Postal Address File (PAF), containing all residential addresses in the boroughs of Lambeth and Southwark, was obtained from the Royal Mail. This is available to all members of the public for a small fee. Approach letters for participation in this study were sent out to a random selection of 355 addresses,

addressed to the occupier, stating the study information and exclusion criteria. Willing parties were asked to contact the study team to register interest.

Addresses were selected at random by assigning each of the 252,927 addresses a number, and then randomly generating 1,000 numbers, from 1 to 252,927. The first 355 addresses were selected from the pool of 1,000 and were sent letters in batches of approximately 30, starting with the first 30 random addresses selected.

From previous experience this method yields a 10% "interested" response rate (Hubbard et al., 2012).

3. A database available to all researchers at the Institute of Psychiatry, MindSearch, which holds details of willing volunteers for human participation studies, was also used. Inclusion and exclusion criteria for healthy participants (as stated below) were sent to the MindSearch organisers. This returned a file containing 585 participants. These participants were all sent an email explaining the study, and willing parties were asked to contact the study team to register interest.

   Inclusion criteria for healthy control participants were:

   - Over the age of 18
   - First language English/very good English speaking ability

   Exclusion criteria for healthy control participants were:

   - Below the age of 18
   - Have suffered from a psychotic episode, or suffer from mild cognitive impairment, Alzheimer's disease or depression.

5.1.2 *Patients with FEP*

First episode psychosis patients were recruited by approaching patients who had completed participation in a study at the Institute of Psychiatry, the European Union – Gene Environment Interaction study, (PI Dr C Morgan). As patients were recruited during their first episode of psychosis, no formal, fixed diagnosis had been made at the time of participation in this study, however all patients met the inclusion listed below.

Part of the study required participants to complete 2 booklets of questionnaires and assessments over 2 or 3 appointments and involvement in the EU-GEI study had ceased following completion of the booklets. The EU-GEI study team asked patients who had completed the two booklets on their final appointment if they would like to take part in another study. If the patient consented to the passing on of his/her details they were approached with a phone call or letter, explaining this study and asking for their participation. If the patient expressed an interest in taking part an appointment was set up to explain the study again and ask for the patient's consent. Once consent was gained the patient was asked to complete the study, as detailed below. Inclusion criteria for psychosis patients were:

- Age 18 to 64
- Presence of an untreated first episode of psychosis (even if long-standing) (ICD-10: F20-29; F30-33 [DSM equivalents: 295.xx to 298.xx]) during the study period (1st January 2010 to 31st May 2013) [n.b. this does not mean that cases have to be untreated at the point at which they are seen, only that treatment (as defined below) was not begun prior to 1st January 2010]

Exclusion criteria for first episode psychosis patients in this study were:

- Age under 18 or over 64
- Treatment for an episode of psychosis outside of the study period

- Evidence of psychotic symptoms precipitated by an organic cause
- Transient psychotic symptoms resulting from acute intoxication as defined by ICD-10
- Have been detained in prison - the study from which these patients were recruited chose to include patients who were in prison at the time of contact and assessment, whereas this study chose not to include any patients who were detained; however any patient who had previously been detained was eligible.

5.1.3 Patients with ED

Early stage dementia patients were recruited through the "Plasma Based Biomarkers for Alzheimer's Disease" study (PI Prof S Lovestone). Patients included in this study were originally recruited from South London and Maudsley (SLaM) memory services and SLaM GP surgeries by Dr Costafreda (second supervisor and Clinical Lecturer in the Department of Old Age Psychiatry), who is part of the clinical care team for this cohort. Once recruited into the study, the research team contacted any participant who met this study's requirements of MCI/mild AD, as long as they could be seen within four months of having an MRI scan. Participants were assessed using a general cognitive test – Mini Mental State Exam (MMSE) - and the tests included in the "Consortium to establish a registry for Alzheimer's disease" CERAD). Patients categorised as ED had scored 1.5 SD (MCI) or 2 SD (early AD) below the normative age adjusted scores in at least one of the following: verbal fluency, Boston naming test, word list memory, constructional praxis, word list recall, word list recognition, word list delayed recall, recall of constructional praxis. The team asked if the patients' details could be passed on to the PhD student. If patients consented to the passing on of their details they were approached with a phone call or letter, explaining this study and asking for their participation. If the patient was interested an appointment was set up to explain the study again and ask for the patients consent. Once consent was gained the patient was asked to complete the study, as detailed below. It is worth pointing out that, while MCI constitutes as a high-risk state for dementia, up to 50% of MCI patients may never progress to overt dementia. That said, as this study is a cross-sectional design it is interested in associations between current functional profile and metacognition rather than longitudinal effects.

The inclusion criteria for patients recruited from the Biomarkers study are stated below:

- MMSE score >=20 and with a clinical diagnosis based on ICD-10 criteria of dementia in AD or MCD (Mild cognitive disorder, the ICD terminology for mild cognitive impairment). This cut off score was decided upon to limit the chance of contacting patients who did not have the capacity to consent. The cut off score is consistent with mild stages of dementia and MCI.
- Patients must have had an MRI in the last 5 months. Due to the degenerative nature of MCI or Dementia, assessing patients who received an MRI over 5 months prior to participation in this study may have resulted in the MRI data being un-representative of the patients' brain structure at the time of assessment.

Exclusion criteria for dementia patients were:

- Mini Mental State Examination (MMSE) score <20.
- Evidently not possessing the capacity to consent. Assessment for capacity to consent was carried out by a research nurse from the Biomarker study team who specialised in old age psychiatry and had specific experience in consenting older adults for research. This was conducted prior to patients' signing the consent form.

Patients were recruited according to the inclusion and exclusion criteria stated above. This particular threshold of MMSE score (>20) included patients with diagnoses of either MCI or mild AD, and thus the group is referred to as "early stage dementia", so as to be inclusive of both diagnoses.

5.1.4 *Depressed patients*

First attempts were made to advertise the study in GP Surgeries in Lambeth, using posters or information sheets. However, after 6 months of contacting suitable surgeries, none agreed to advertise the study. The study description was therefore added to the King's College, London Research Studies page (https://internal.kcl.ac.uk/innovation/studies/index.aspx), which advertised the study for 2 months, featuring in two of the advertising circular emails, sent to staff and subscribers. Potential participants registered interest via email or phone.

Inclusion criteria for depressed patients were:

- Over the age of 18.
- Score >=14 on the Beck Depression Inventory at the time of registering interest.
- Have a formal diagnosis of Depression (by a GP/Psychiatrist/IAPT practitioner; diagnosis from the patients' own report; no access to medical records was required).

Exclusion criteria for depressed patients were:

- Under the age of 18.
- Have a history of psychotic disorders, mild cognitive impairment or Alzheimer's disease.
- Score of <14 on the Beck Depression Inventory at the time of registering interest.

This patient group was required only for the between-group comparisons, reported in chapter 10.

5.2 Participant numbers

All participants had normal or corrected-to-normal vision. There were 73 healthy adults included (31 men, 42 women); 20 patients with first episode of psychosis (12 men, 8 women); 18 patients with ED (11 men, 7 women); and 15 patients with Depression (5 men, 10 women).

5.3 ETHICAL APPROVAL

Ethical approval for healthy participant participation was granted by the Psychiatry, Nursing and Midwifery research sub-committee of King's College, London Research Ethics Committee (REC ref: PNM/11/12-94). Ethical approval for patient participation was granted by the NHS National Research Ethics Service Committee London – Fulham (REC ref: 13/LO/0661).

5.4 BEHAVIOURAL MEASURES

5.4.1 METACOGNITION MEASURES

Perceptual metacognitive efficiency

Perceptual metacognitive efficiency was investigated using a computerised visual perceptual metacognition task, similar to that used in the study by Fleming et al. (2010). Each trial required participants to perform a perceptual task. The stimuli used were Gabor patches: circular patches of alternating light and dark vertical bars (2.8 visual degrees in diameter, spatial frequency of 2.2 cycles per visual degree). The contrast between the vertical lines in each standard Gabor patch was 20%, where 0% indicates no difference between the light and dark bars and 100%, the maximum difference (black to white). Six such Gabor patches were arranged in a circle (eccentricity of 6.9 visual degrees) around a central fixation point (see figure 5.4-1a). One of the six Gabor patches could be made to pop-out from the others by increasing the contrast in that patch compared with the standard 20% contrast of the others. The contrast of the pop-out Gabor patches varied from 23% (little effect of pop-out) to 80% (pop-out very clear). The task required participants to view two stimulus arrays, each presented for 200 ms, separated by an interval of 300 ms.

Each array contained the six Gabor patches around a central fixation point, set against a uniform gray background. The interval between stimuli comprised a uniform gray screen without the Gabor patches. A single Gabor patch in one of the two intervals was designated as a pop-out. Which of the six Gabor patches popped-out varied randomly between trials.

Participants were prompted by a computer display to respond “1” or “2” (presented centrally) as to whether they thought the pop-out Gabor patch appeared during the first or second presentation. Participants responded by pressing the numerical keys on the top left-hand side of the laptop keyboard with their left hand, with a red box surrounding their response. Participants had 2 s in which to make their decision; if an answer was not given in this time the phrase “Too Slow” appeared on the screen. No feedback was given as to whether responses were right or wrong.

Participants then indicated confidence in their decision on a scale of 1–6 (1: relatively low confidence; 6: relatively high confidence; see Fig. 5.4-1a). The display screen consisted of the numbers 1–6 presented centrally. Participants were encouraged to use the full range of the scale, thinking carefully about how confident they were after each decision. Participants responded by pressing numerically marked keys on the top left-hand side of the laptop keyboard with their left hand, with a red box again surrounding this selection. Participants had 3.5 s to complete this metacognitive judgement. Performance on the task was maintained at around 70% using a 2-down, 1-up staircase procedure (Levitt, 1971). Two consecutive correct visual judgments led to a one step (3%) decrease in contrast of the pop-out Gabor patch in the next trial, whereas one incorrect visual judgment led to a one step increase in contrast of the pop-out patch. This procedure ensures all participants perform with approximately the same accuracy on the primary perceptual task, allowing us to measure metacognitive efficiency independent of task performance. This was especially useful in the present study, as the range of participant ages may otherwise have led to performance bias. Older participants who struggled to make manual responses in the time permitted gave verbal answers to the researcher who made manual responses. The task comprised 5 blocks of 8 minutes with short breaks between each block, taking approximately 50 minutes to complete.

A standard task instruction sheet explaining the task was read through by participants on their own, they were then given the opportunity to ask the task administrator questions. Participants were seated in a darkened room approximately 60 cm from a laptop computer screen (Sony Vaio, PCG-71614M laptop; 17 in display; 1280 x 800 pixels). Stimulus display and responses for the tasks were programmed in MATLAB 7.8 (Mathworks Inc., Natick, MA, USA; using the COGENT 2000 toolbox (http://www.vislab.ucl.ac.uk/cogent.php). A practice session of two blocks of eight trials was given at the start to familiarise participants with the task. Participants were tested individually in a quiet room. All 54 participants completed the perceptual metacognition task as used in the study by Fleming et al. (2010). As this task requires more sustained attention from participants it was decided to complete this first to avoid fatigue effects confounding the data, especially in older participants. Participants are asked to sit in front of a laptop computer screen, which was no further than 20cm from the edge of the surface on which it is placed. The experimental task had 5 blocks of 8 minutes, with short breaks in between each block, therefore taking approximately 50 minutes to complete.

Participants were firstly presented with a practice session. The trials in this session were easier, and the contrast between pop-out and non-pop-out patches was much more obvious than in the experimental trials. The time they were given to make their responses was also longer than in experimental trials.

Participants over 60 years old were asked to complete a slightly easier version of the experimental task, where the staring contrast of the Gabor patches was higher and therefore easier to see, with additional response and stimuli presentation times. These modifications were in place to compensate for general age related decline in response times and visual perception ability.

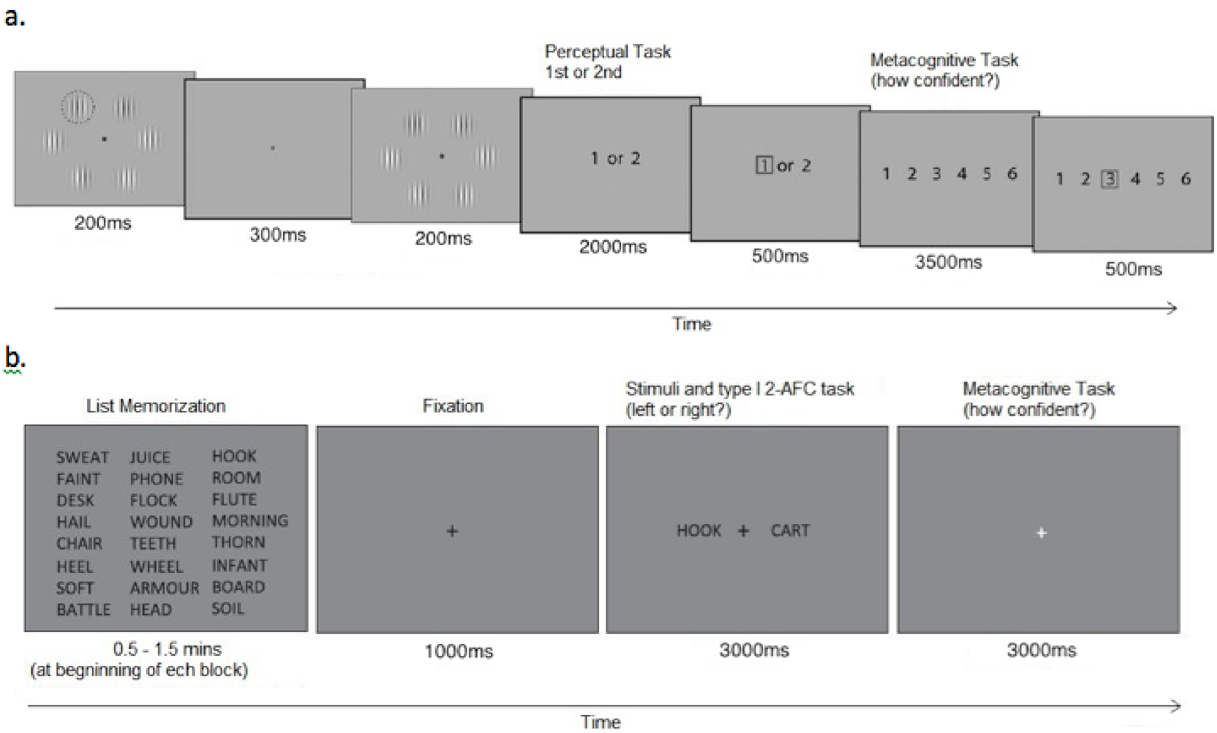


Figure 5.4-1. a) Visual Perception Metacognitive task; 1 trial (adapted from Fleming et al, 2010). b) Memory Metacognition task, 1 trial (adapted from McCurdy et al, 2013)

Memory metacognitive efficiency

Memory metacognitive efficiency was investigated using the 2-AFC memory confidence task devised by McCurdy et al. (2013; see figure 5.4-1b). At the beginning of each block 50 English words (Calibri font, size 24; appendix 5.1) were presented simultaneously on the screen for 0.5, 1, or 1.5 min to create three levels of difficulty to ensure that, overall, participants performed at neither chance nor ceiling; analysis did not involve comparing the different levels of difficulty. English words were generated using the Medical Research Council Psycholinguistic Database (Wilson, 1988). These standard nouns were four to eight letters long, had one to three syllables, and had a familiarity, concreteness, and imagability rating of 400–700 each. Participants were instructed to memorize as many words on the list as possible during the study period. A small notice appeared at the bottom of the screen to inform them when there was 10s left to study the list. After the study period, a series of trials probing memory for the word list was presented. In each trial, two words were presented to the left and right of fixation. One of these words had been presented on the study list ("old"), and the other word had not been presented previously ("new"). First, participants had 250ms to provide a 2-AFC judgment with regard to which word was "old", where pressing "1" referred to the left hand word and "2" referred to the right hand word. Participants had 250ms seconds to press one of four keys ("7," "8," "9," or "0") using their right hand to indicate their confidence in being correct about their memory judgment (signifying "not at all confident" to "very confident" respectively). Older participants who struggled to make manual responses in the time provided gave verbal answers to a researcher who made manual responses. The task comprised 3 blocks of approximately 5 minutes each with short breaks in between each block. 34 participants completed the memory metacognition task.

5.4.2 Calculating metacognitive efficiency

Metacognitive efficiency was quantified using the meta d'/d' measure developed by Maniscalco & Lau (2012). It is known that other measures of metacognitive ability are affected by primary task performance (Galvin et al., 2003; Maniscalco & Lau, 2012). For example, if two individuals A and B have identical metacognitive ability, but A performs better than B on the primary task, A's metacognition score will appear higher than B's due to this performance confound. Calculating meta d' circumvents this issue. As meta d' is expressed in the same units as task performance (*d'*), we can construct a relative measure of metacognitive efficiency (meta d'/*d'*) to isolate metacognition from variations in task performance. Importantly, meta d'/*d'* is a relative measure: given a certain level of processing capacity (*d'*), meta d'/*d'* quantifies the extent to which a metacognitively optimal observer is aware of their performance (discussed previously in chapter 2.2)

5.4.3 *Mood ratings*

A simple and frequently used method of self-rating a characteristic or attitude, in both clinical and research settings, is a visual analogue scale (VAS; Wewers and Lowe, 1990). This type of scale was used in the present study to measure participants' current subjective mood. The scale asks participants to rate how happy they are, ranging from 1=very unhappy to 10=very happy (see appendix 5.1). There were no other marks on the scale; this was so participants were encouraged to use the entire width of the line and avoid responses clustering around specific points, such as the mid-point. This took no longer than one minute to explain and carry out.

The Beck Depression Inventory (BDI; Beck & Steer, 1984; see appendix 5.2) is a common measure of depression, and is widely used in both the clinical and non-clinical populations (Lasa et al., 2000). The BDI is a 21-item self-report questionnaire designed to assess the presence and severity of symptoms of depression over the previous 2 weeks. Each of the 21 items corresponds to a symptom of depression, and scores are totalled to give a single overall score. There is a four-point scale for each item ranging from 0 to 3. The pilot study confirmed our assumption that most participant scores would fall within the "normal" or "minimal" range with scores of 0-13; scores of 14-19 are classed as mild, 20-28 as moderate, and 29-63 as severe.

5.4.4 *Measures of insight*

Cognitive insight ratings were measured in all participants using the Beck Cognitive Insight Scale (BCIS; Beck et al, 2004; appendix 5.3). The BCIS is a 15-item self-report questionnaire that assesses participants' self-reflectiveness and overconfidence in their interpretations of their experiences. There is a four-point scale for each item ranging from 1 to 4. The questionnaire can be split into two subscales; self-reflectiveness (SR; 9 items) and self-certainty (SC; 6 items). This scale was designed with the aim of identifying possible thinking biases, rather than skill deficits. Recent research (Kao et al, 2011; Martin et al, 2010) has shown that the scale is reliable and suitable for use in the general population as well as with psychiatric patients. The scale was selected to allow for direct comparisons to be made between the general population and patients in this study (see chapter 6 for factor analysis and meta-analysis).

Insight into executive deficits and behaviour was measured in all participants using the Dysexecutive Questionnaire (DEX; appendix 5.4). The DEX is a 20-item measure of participants' opinions about their executive and cognitive functions, and how these impact on their daily life, e.g. "I lose my temper at the slightest thing" and "I will say one thing, but do something different". An Independent rater (IR) is required to complete a separate version of this questionnaire, where they answer questions about the participant (these questions are identical to those the participant has answered about themselves). Ideally the IR will be a spouse or person living with the participant, as an accurate and objective measurement of the participants' dysexecutive abilities is required, as well as the subjective report of the participant. Discrepancy scores between the participants' own ratings and the IR's ratings about the participant are calculated by subtracting participant scores from the IR scores. A greater difference in scores leads to a larger discrepancy, where a negative value indicates that participants are unaware and underestimating their cognitive dysfunction, and a positive number indicates participants are overestimating their level of cognitive dysfunction. A larger discrepancy score therefore indicates that participants have less insight into their illness, as they have overestimated or underestimated their functioning compared to the objective, more accurate view. Research (Chan, 2001) has shown that this scale is reliable and suitable for use in the general population as well as with psychiatric patients. This took no longer than 5 minutes to complete.

Clinical insight scores, from patients (Psychosis, Dementia and Depression) only, were measured using the Schedule for the Assessment of Insight - Expanded (SAI-E), (Kemp and David, 1997). This is a simple semi-structured clinician-administered series of questions on the three dimensions of insight (ability to recognise illness, ability to relate their unusual mental events as pathological, and compliance with medication; David, 1990), which are rated on three levels, and measures patients' awareness of change, and its effects on their functioning.

5.4.5 NEUROPSYCHOLOGICAL MEASURES

The Wechsler Memory Scale (WMS; appendix 5.6) logical memory task (Wechsler, 1997a) is designed to detect attention and memory deficits, and is suitable for use in participants from 16-90 years of age. The "logical memory" task asks participants to listen to and remember a spoken story. Stories were recorded in a quiet room on iPhone 4S Voice Memo application. They were presented to each participant using iPhone 4S speakers to ensure all participants heard the same story presented in exactly the same way. After hearing each story participants were then asked to recount the story to the researcher, and obtained scores for remembering key facts and aspects of the story. The more aspects of the story remembered, the higher the participants' score. Story A is played once to the participant who then recalls any information they can remember. Story B is played twice (B-I and B-II), with the participant recalling information after each reading. After 30 minutes from when the stories are initially played to the participants they are asked again recount the stories to the researcher (A2, B2; total recall after 30 minutes). A recognition task is then carried out, where participants are asked 15 questions about each of the stories and required to give "Yes" or "No" answers.

Scores are derived from the learning slope (difference between number of items recalled on Story B-I and Story B-II), total immediate recall (story A score + story B-II score), total recall after 30 minutes (story A2 score + story B2 score), recognition score (recall score on A + recall score on B) and total percentage information retained ([immediate recall/30 min recall] *100). The scores reported in this thesis are the raw memory scores, not age adjusted. Age adjusted scores give a score of an individuals' memory ability compared to their age-group norms. The use of raw scores in this study therefore gives us an individuals' absolute memory scores rather than a view of their memory ability compared to age-related norms. Given there is a small but significant age-related decline in memory ability, and the participants included in this sample have a wide age range, the use of raw scores may appear to inflate the difference between memory abilities between and within groups across the age range, thus affecting the interpretation of results.

The abbreviated Wechsler Adult Intelligence Scale (WAIS; Wechsler, 1997b; appendix 5.7) measures IQ. This takes the digit symbol coding, arithmetic, block design and information sections from the full WAIS-III battery of assessments that creates a scaled IQ score. This shortened version of the WAIS-III was selected because it only takes approximately 20 minutes with healthy controls, and 30 minutes with patients, whilst still providing a reliable measure of their IQ. This was required since an aim of this study is to establish whether overall intellectual ability correlates with metacognitive efficiency.

The Trail Making Test is designed to measure the cognitive domains of processing speed, sequencing, mental flexibility and visual–motor skills (Bowie and Harvey, 2006; appendix 5.8). The test comprises of two parts; A and B. Part A requires the participants to connect a series of 25 numbers outlined with a circle in ascending numerical order. This part of the task is designed to be a simple test of visual search and motor speed skills. Part B of the task requires the same connecting of circles but instead participants have to ascend in number and letter order (1-A-2-B-3-C—etc.). This part of the task is designed to also be a test of higher-level cognitive skills, particularly task switching, aspects of executive control (Bowie and Harvey, 2006).

In each task the numbers (and letters) are placed in a semi-random fixed order to avoid overlapping connector lines. The score of interest is the completion time, especially that of B. A score of basic task speed and attention is obtained using A; we can then remove the effect of general speed from task B by subtracting time A from time B (Trails B-A score). If executive function is intact a faster B-A value is anticipated.

The Brixton Test is a sub-test developed within the Hayling and Brixton tests of executive functioning (Burgess and Shallice, 1997; appendix 5.9). The test presents participants with a 56-page stimulus booklet. Each page contains 2 rows of 5 circles, where each circle is numbered from 1 to 10. On each page one of these circles is blue. The position of the blue circle can change on each page. Changes depend on a set of rules, which can change without warning to the participant. Participants are required to point out where they think the next blue circle will appear, with the intention being for participants to work out and use the rules using previous pages. Responses are considered correct if participants follow the current rule. Where a rule has changed, they answer correctly if they continue to use the rule from the previous page. Scores are obtained by noting the number of errors, where the maximum number of errors that can be made is 55. A higher score reflects poorer performance and therefore poorer executive function.

Verbal Fluency task (FAS; Spreen & Benton, 1977; appendix 5.10) asks participants to list words, either beginning with a specific letter (phonological fluency; F A and S) or those belonging to specific categories (Fruit, Parts of the Body and Animals) within a 1-minute limit. The number of correct and incorrect words (non-word, not belonging to that category/letter group, name, place or number) and repeated words are tallied for both the first 30 seconds and the total 60 seconds. This is regarded as an executive function test since it requires word generation, maintenance of set and the monitoring of previous responses to prevent repetitions and out of category items.

5.5 STATISTICAL ANALYSIS

All analyses were performed using SPSS v.22 (SPSS Inc., 2013). As data were continuous and normally distributed, parametric tests were used.

5.5.1 WITHIN-GROUP ANALYSES

Pearson's Correlation analyses were carried out to compare variables within each individual group. Specifically, the following associations were investigated:

- The relationship between both domains of metacognitive efficiency (perception and memory) and age, measures of mood (VAS and BDI) and neurocognition.
- The relationship between measures of insight (BCIS sub-scales, DEX sub-subscales and the SAI [for patients only]) and mood.
- The relationship measures of insight and both domains of metacognitive efficiency scores.

5.5.2 BETWEEN-GROUP ANALYSES

ANOVAs were carried out to compare variables across the younger participant groups: 1) Healthy adults less than 60 years of age, 2) FEP patients, and 3) depressed patients. Scheffé's post-hoc tests were performed to identify the difference between individual groups, as opposed to the less conservative least significant difference (LSD) post-hoc test. Specifically, the following comparisons were carried out:

- The difference in scores of cognitive insight (BCIS sub-scales) and awareness of executive and behavioural deficits (the DEX-sr).
- The difference in scores of metacognitive efficiency. Due to the small number of FEP patients who successfully completed the perceptual metacognitive task, these data were not included in the between-group comparison.

T-test analyses were carried out to compare variables across both the older participant groups: 1) Healthy adults of 60 years and over, 2) ED patients, and across the two patient groups. Specifically, the following comparisons were completed:

- The difference in scores of cognitive insight (BCIS sub-scales) and awareness of executive and behavioural deficits (the DEX-sr).
- The difference in scores of memory metacognitive efficiency. Due to the small number of patients in both groups who successfully completed the perceptual metacognitive task, these data were not included in the between-group comparison.

5.6 PROTOCOL

Where possible the following order of task presentation was carried out. If participants reported being fatigued, or requested shorter sessions, the protocol was split into two parts of approximately 1 hour each.

1. The experiment was first described briefly to participants and any questions they had were answered, without disclosing the nature of the computerised assessments. Consent was then obtained.

2. Basic information was then collected regarding age, ethnicity, education, employment and relationship status. This task took no longer than one minute to explain and carry out.

3. Participants were then asked to rate their current mood on a Visual analogue scale (VAS). This task took no longer than one minute to explain and carry out.

5. Participants were then asked to complete the perception metacognitive task. This task took no longer than 50 minutes to complete.

6. Participants were then asked for a second time to rate their mood on the VAS.

7. Participants were then asked to complete the BDI. This task took no longer than 5 minutes to complete.

8. Participants were then asked to complete the BCIS. This task took no longer than 5 minutes to complete.

9. Participants were then asked to complete the DEX. This task took no longer than 5 minutes to complete.

10. Patients only were then asked to complete the SAI-E. This task took no longer than 10 minutes to complete.

11. Participants were then asked to complete the first part of the WMS. This task took no longer than 10 minutes.

12. Where necessary the WAIS was administered. (Some participants had already completed this battery of assessments for a previous study and hence did not need to complete it, instead obtaining scores from the previous study.)

13. The Trail Making Task was then administered. This task took no longer than 5 minutes to complete.

14. The Brixton Spatial Anticipation Test (Brixton test) was then administered. This task took no longer than 5 minutes to complete.

15. The verbal fluency task was then administered. This task took no longer than 10 minutes to complete.

16. The second half of the WMS was then carried out. This task took no longer than 10 minutes to complete.

17. The memory metacognition task was then administered. This task took no longer than 15 minutes to complete.

18. Participants were then debriefed and any questions answered. Payment of £10 was then given.

Mood induction

An initial aim of the study was to investigate the effect of mood induction on healthy participants' metacognitive abilities using Velten statements (Velten, 1968). However, the induction procedures did not have any significant effect on participants' mood, and hence this portion of the study was set aside.

5.7 Additional measures – ED

ED patients were recruited from a larger study at the Institute of Psychiatry and therefore had already completed some relevant assessments, the results of which were made available along with the data collected by this study.

The MMSE (Folstein, Folstein, & McHugh, 1975) is the most commonly used test for complaints of memory problems, and is commonly used to help diagnose MCI and dementia, and follow progression of memory complaints over time. It is a 30-point assessment that measures: Orientation to time (what time and date is it), Orientation to place (where are you now, nearby street etc.), Registration (repeating named words), Attention and calculation (Count back from 100 in sevens/ spell "world" backwards). Recall of registration words, Language (name a pencil and a watch), Repetition (speaking back a phrase) Complex commands (draw picture or complete a set of written commands). Regarding scores, 27-30 represents “normal cognition”, below this score represents mild (19-26), moderate (10-18) or severe (0-9) impairment. That said, a score of 27-30 does not rule out the presence of MCI. The assessment can take between 10 and 15 minute to complete.

For the current study an MMSE score of less than 30 and failure on one section of the CERAD or Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-Cog) was used to determine inclusion, data from which was no included in the analyses of this thesis.

CHAPTER 6

6. RELATIONSHIP BETWEEN THE BCIS AND DEPRESSION: A META-ANALYSIS

6.1 BACKGROUND

The Beck Cognitive Insight Scale (BCIS) literature has been covered in Chapter 3.2 and its properties in Chapter 5.4.4.

The rationale for this meta-analysis was that, in addition to metacognition and neurocognition, mood is also one of the more robust predictors of clinical insight, with lower mood tending to be related to improved insight, as well as a narrative review, highlighting a potential link (see Chapter 3; Mintz, et al., 2003; Riggs et al., 2012). As BCIS scores are known to be positively associated with measures of clinical insight (Riggs, 2012), and be similarly positively associated with positive symptoms (Engh et al., 2010; Ouzir, Azorin, Adida, Boussaoud, & Battas, 2012; Warman et al., 2007; Riggs, 2012) it is predicted that cognitive insight may also be positively associated with depression scores. Further, as covered in chapter 3.2, Granholm et al. (2005) have suggested that better cognitive insight may be the result of low mood, due to changes in self-perception.

Existing literature therefore indicates that further review of this relatively new insight measure should be carried out to investigate the mood/cognitive insight relationship. The aim of this chapter was to collate data from all available papers that reported both cognitive insight and depression scores in patients with schizophrenia, from 2004-2013, and perform a meta-analysis to examine the relationship between mood and cognitive insight. The hypothesis tested stated that 'the relationship between mood and cognitive insight will demonstrate an overall positive association between self-reflection and depression'.

6.2 Method

6.2.1 Design

This study identification strategy had two phases. PubMed and Web of Science databases were searched for relevant papers using the search terms COGNITIVE INSIGHT or BCIS or "BECK COGNITIVE INSIGHT SCALE" combined with PSYCHOSIS or SCHIZOPHRENIA combined with DEPRESSION or MOOD or AFFECT. This generated 135 results from PubMed and 344 results from Web of Science. The returned papers were then screened using the following inclusion criteria: (1) Correlations between BCIS and Depression (Hamilton Depression Scale [HDRS], Beck Depression Inventory [BDI], Calgary Depression Scale [CDS], Positive and Negative Symptom Scale (depression item) [PANSS]) were reported in the study or sufficient information was reported to enable us to compute effect sizes; (2) the sample comprised patient groups with a psychotic disorder (first-episode psychosis, schizophrenia, schizoaffective disorder), (3) the article had been published in a peer-reviewed English-language journal; 4) the article had been published before October 2013.

Of the papers returned in the literature search, 19 met the inclusion criteria, (see Table 6.1-1) 14 of which were included in the analysis. Some of the studies identified in this literature search could not, unfortunately, be included (Lepage et al., 2008; Penn et al. 2009; Bucy et al., 2010; Ekinci, Albayrak, and Ekinci, 2012; Ekinci & Ekinci, 2013). This was due to a lack of reporting of specific mood/cognitive insight relationships. Despite our best efforts to obtain the information via email or phone not all sets of data were acquired. We also acknowledge that some relevant studies may, unfortunately, have been missed in the literature search where the data were part of a study whose focus was not insight.

Study name	Sample size	BCIS measure used	Depression Measure	Mean Age (years)
***Beck et al. (2004)**	75	SR, SC, CI	BDI	38.92
***Pedrelli et al. (2004)**	164	SR, SC, CI	HDRS	53.3
***Granholm et al. (2005)**	39	SR, SC, CI	HDRS	54
***Colis et al. (2006)**	150	SR, SC, CI	BDI	36.2
***Warman et al. (2007)**	50	SR, SC, CI	BDI	40
Lepage et al. (2008)	55	SR, SC, CI	CDS	23.2
Penn et al. (2009)	65	SR, SC, CI	BDI	40
***Uchida et al. (2009)**	30	CI	BDI	26.7
Buchy et al., (2010)	61	SR, SC, CI	CDS	23.4
***Greenberger and Serper (2010)**	50	SR, SC, CI	CDS	47.3
***Gilleen, Greenwood, and David (2011)**	29	SR, SC, CI	BDI	38.3
***Kao, Wang, Lu, and Liu (2011a)**	118	SR, CI	BDI	39.3
Buchy et al., (2012)	44	SR, SC, CI	CDS	23.3
Ekinci, Albayrak, and Ekinci (2012)	121	SR, SC, CI	CDS	37.8
***Ekinci, Ugurlu, Albayrak, Arslan, and Caykoylu (2012)**	100	SR, SC, CI	CDS	36.8
***Mass et al. (2012)**	88	SR, SC, CI	CDS	34.8
***Tastet, Verdoux, Bergua, Destaillats, and Prouteau (2012)**	53	SR, SC, CI	BDI	33.8
Ekinci and Ekinci (2013)	133	SR, SC, CI	CDS	36.4
***Raffard et al. (2013)**	60	SR, SC	BDI	36.8
***Wiffen (2011)**	90	SR, SC, CI	PANSS	29.3

Table 6.1-1 Table of all identified studies using BCIS and Depression measures, including their sample size, sub-scales included, depression measure used and mean participant age. Studies included in this analysis are indicated with an * next to the authors.

Data from each paper were separated into the three sub categories of BCIS: self-reflection (SR), self-certainty (SC) and composite index (CI). A database was created in which all relevant characteristics of each included study were stored: authors, publication year, sample size, mean sample age, sub-scales of BCIS used, measure of depression used (to potentially differentiate between effects of different scales), type of analysis run, p value, r value, group means and effect direction. If the effect size could not be determined by the information in the study then attempts were made to locate the primary author of the study and request the information.

6.2.2 *Data analysis*

All analyses were completed in Comprehensive Meta-analysis package version 2. We used correlation (r) or mean group data combined with sample size and effect direction to calculate the effect size for each study. After inputting relevant data for each study a combined effect weighted for sample size was calculated for the three BCIS measures (SR, SC and CI) separately. Z and p values provide an indication as to the statistical significance of the association. In order to account for the heterogeneity of measures, a random-effects model was used (Borenstein, Hedges, Higgins, & Rothstein, 2010).

Publication bias was examined by using a funnel plot of standard error and Fisher Z score. Using the "Duval and Tweedie's Trim and Fill" (Rothstein, Sutton, & Borenstein, 2006) procedure, putatively missing studies (as inferred from an asymmetric plot revealing bias due to small studies with positive correlations) were imputed and added to the funnel plot by an iterative procedure.

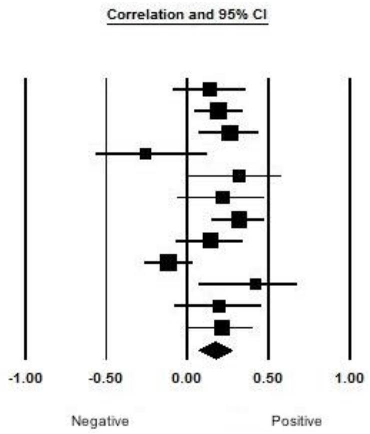
6.3 Results

14 studies were included in the current meta-analysis, while the number of patients included depended on the studies included in each analysis. The mean age across studies was 40.1 years (accounting for varying sample sizes), with an age range from 26.7-54.5 years, resulting in a range of 27.8 years. The smallest sample size was 29 (mean age 38.3), the largest was 164 (mean age 53.3).

6.3.1 *Composite Index*

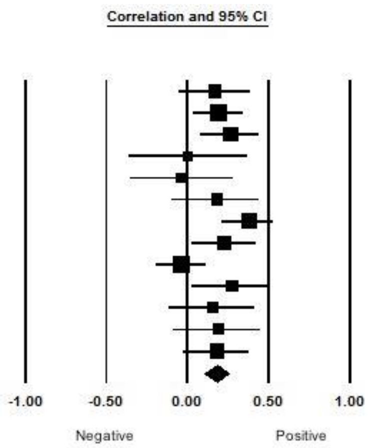
929 patients were included in this analysis from 12 studies. There was a small but significant positive correlation between the CI subscale of the BCIS and depression scores ($r=.134$, $p<.04$, $z=2.059$; see figure 6.3-1a). This suggests those patients with higher depression scores also possess higher overall cognitive insight. However, this effect appears to be strongly driven by the effect of depression on SR (see below).

Study name	Subgroup	Correlation	Lower limit	Upper limit	Z-Value	p-Value
Beck 2004	CI	0.140	-0.090	0.356	1.196	0.232
Colis 2006	CI	0.194	0.038	0.341	2.431	0.015
Ekinci 2012a	CI	0.261	0.068	0.435	2.631	0.009
Gilleen 2011	CI	-0.255	-0.568	0.123	-1.330	0.184
Granholme 2005	CI	0.320	0.005	0.577	1.990	0.047
Greenberger 2010	CI	0.220	-0.062	0.470	1.533	0.125
Kao 2011	CI	0.320	0.148	0.473	3.557	0.000
Mass 2012	CI	0.140	-0.072	0.339	1.299	0.194
Pedrelli 2004	CI	-0.120	-0.268	0.034	-1.530	0.126
Uchida 2009	CI	0.420	0.070	0.678	2.326	0.020
Warman 2007	CI	0.198	-0.085	0.451	1.376	0.169
Wiffen 2011	CI	0.210	0.003	0.400	1.988	0.047
		0.172	0.071	0.269	3.327	0.001



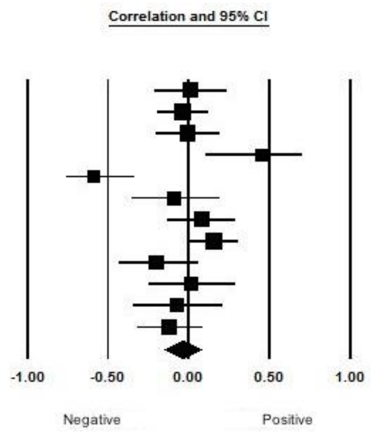
a.

Study name	Subgroup	Correlation	Lower limit	Upper limit	Z-Value	p-Value
Beck 2004	SR	0.170	-0.059	0.382	1.457	0.145
Colis 2006	SR	0.192	0.036	0.339	2.404	0.016
Ekinci 2012a	SR	0.267	0.074	0.440	2.695	0.007
Gilleen 2011	SR	0.000	-0.367	0.367	0.000	1.000
Granholme 2005	SR	-0.040	-0.351	0.279	-0.240	0.810
Greenberger 2010	SR	0.180	-0.104	0.436	1.248	0.212
Kao 2011	SR	0.378	0.212	0.523	4.265	0.000
Mass 2012	SR	0.230	0.022	0.419	2.159	0.031
Pedrelli 2004	SR	-0.040	-0.192	0.114	-0.508	0.612
Raffard 2013	SR	0.274	0.022	0.494	2.123	0.034
Tastet 2012	SR	0.155	-0.120	0.408	1.105	0.269
Warman 2007	SR	0.194	-0.089	0.448	1.347	0.178
Wiffen 2011	SR	0.180	-0.028	0.373	1.697	0.090
		0.178	0.103	0.251	4.626	0.000



b.

Study name	Subgroup	Correlation	Lower limit	Upper limit	Z-Value	p-Value
Beck 2004	SC	0.010	-0.217	0.236	0.085	0.932
Colis 2006	SC	-0.040	-0.197	0.120	-0.488	0.626
Ekinci 2012a	SC	-0.009	-0.205	0.188	-0.089	0.929
Gilleen 2011	SC	0.451	0.101	0.702	2.478	0.013
Granholme 2005	SC	-0.590	-0.763	-0.337	-4.066	0.000
Greenberger 2010	SC	-0.090	-0.359	0.193	-0.619	0.536
Mass 2012	SC	0.080	-0.132	0.285	0.739	0.460
Pedrelli 2004	SC	0.160	0.007	0.306	2.048	0.041
Raffard 2013	SC	-0.200	-0.432	0.057	-1.531	0.126
Tastet 2012	SC	0.017	-0.252	0.283	0.121	0.903
Warman 2007	SC	-0.073	-0.344	0.210	-0.501	0.616
Wiffen 2011	SC	-0.120	-0.319	0.089	-1.125	0.261
		-0.035	-0.148	0.079	-0.597	0.550



c .

Figure 6.3-1 Random effects forest plot of all included studies reporting a) CI values. b) SR values. c) SC values

6.3.2 Self-Reflection

1012 patients were included in this analysis from 13 studies, which indicated that there is a small but significant positive correlation between SR and depression scores (r=.138, p<.02; z=4.287). Patients with higher depression scores show increased self-reflectiveness (see figure 6.3-1b).

6.3.3 *Self-certainty*

1043 patients were included in this analysis from 12 studies. There was no significant relationship between SC and depression scores (r= -.025, p=.683, z=-.409; see figure 6.3-1c)

6.3.4 *Effect of depression scale*

We investigated whether the type of scale used to measure depression had a significant effect on the size of the depression-SR relationship (see figure 6.3-2). The Beck Depression Inventory-II (BDI) questionnaire was the most commonly used measure: 8 of the 13 studies included in the SR analysis. The Calgary Depression Scale (CDS) and Hamilton Depression Rating Scale (HDRS) scales were used in only 2 studies, and the Positive and Negative Syndrome Scale (PANSS) depression measure was only used once. The highest overall correlation and most significant effect was seen between SR and the CDS (r=.239, p<.004), followed by the BDI (r=.229, p<.001). Neither the HDRS (r=-.040, p=.574) nor the PANSS depression item (r=.18, p=.09) had a significant relationship with SR.

The impact of statistical heterogeneity of the different depression rating scales was assessed using the I^2 calculation, which describes the percentage of variation across studies that is due to heterogeneity rather than chance (Higgins, Thompson, Deeks, & Altman, 2003). As the number of studies included in our analysis was low this statistic I^2 was deemed to be more suitable than Cochrane's Q, which is known to be poor at identifying true heterogeneity among studies as significant (Higgins et al., 2003). Overall I^2 = 31.77, which indicates that there is approximately a 32% chance that there was a significant impact of heterogeneity on the results of the meta-analysis. This level is not deemed to be significant in meta-analysis research (Higgins et al., 2003; see table 6.3-1).

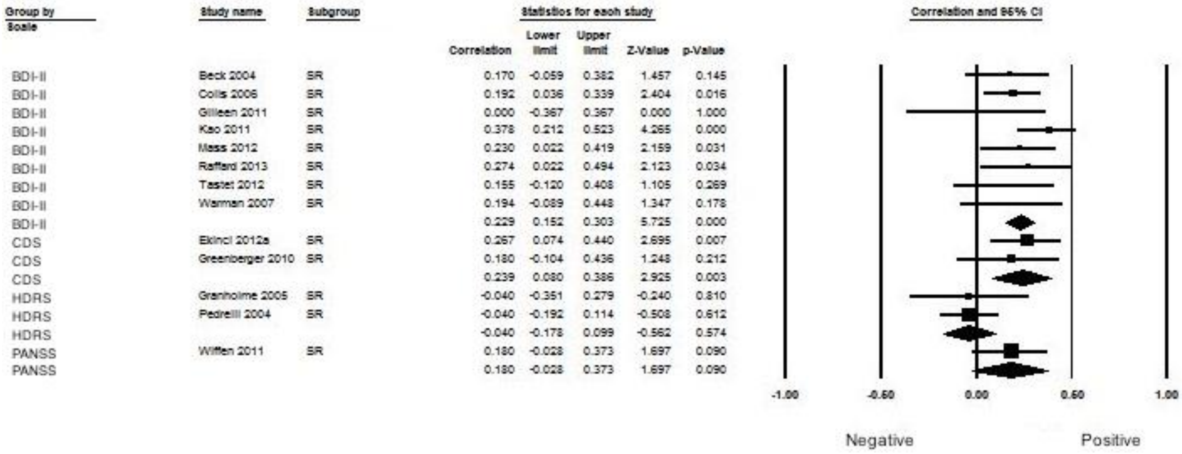


Figure 6.3-2 Random effects forest plot of all included studies reporting SR vales, separated by Depression scale.

Study name	Correlation	Scale
Granholm et al., (2005)	-0.04	HDRS
(Pedrelli et al., (2004)	-0.04	HDRS
Gilleen, Greenwood, & David, (2011)	0	BDI
Tastet et al., (2012)	0.155	BDI
Beck et al., (2004)	0.17	BDI
Greenberger & Serper, (2010)	0.18	CDS
Wiffen, (2011)	0.18	PANSS
Colis et al., (2006)	0.192	BDI
Warman et al., (2007)	0.194	BDI
Mass et al., (2012)	0.23	BDI
Ekinci, Ugurlu, et al., (2012)	0.267	CDS
Raffard et al., (2013)	0.274	BDI
Kao et al., (2011a)	0.378	BDI

Table 6.3-1 Pearson's correlation coefficient for relationship between depression and BCIS SR from smallest to largest, and depression scale.

6.3.5 Publication bias

Publication bias can be detected by observing whether the bottom of the funnel plot (see figure 6.3-3) contains a higher concentration of studies on one side of the mean than on the other. This is not apparent in Figure 6.3-3, therefore it is unlikely that publication bias present in this study. However, due to the low number of studies included this should be interpreted with caution.

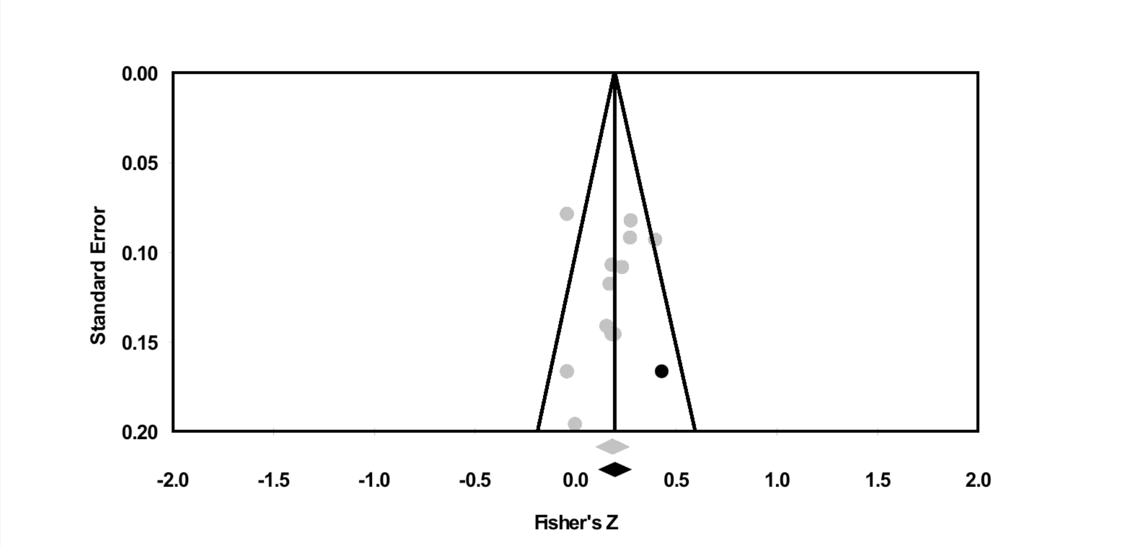


Figure 6.3-3 Funnel plot of standard error by Fisher's Z, included studies in grey, and imputed studies in black.

6.3.6 *Trim and Fill*

Duval and Tweedie's Trim and Fill analysis was run to impute missing studies - another aspect of publication bias. The plot (see figure 6.3-3; actual in grey, imputed in black) demonstrates that only one study is estimated to be missing from this analysis (black circle), and there is minimal change in the diamond average Z score that would arise if imputed studies were included in the analysis.

6.4 Discussion

This meta-analysis sought to provide a preliminary overview and summary of research, published between 2004-2013, on the relationship between cognitive insight and mood in psychotic disorders. The main aim was to investigate if the well-established relationship with mood and clinical insight is also evident with cognitive insight, more specifically was mood related to SR scores.

Our analysis of results from 14 studies supported the hypothesis that there would be an "overall positive association between self-reflection and depression", and demonstrated that there was a small but highly significant effect of mood on the BCIS composite index in schizophrenia, which was driven by the self-reflectiveness sub-scale. There was no significant effect of mood on SC scores. Hence, greater capacity to self-reflect is associated with worse mood, however whether this is cause or effect is still to be determined. This finding echoes one of the more robust findings in the insight literature, which is the frequent observation of a link between greater clinical insight and worse mood (Mintz et al., 2003), and therefore implies that while the two forms of insight are conceptually separate they are, at least in part, related by the SR subscale and its relationship with affect. The effect sizes found in both the Mintz et al. (2003) analysis of clinical insight and the current paper are also very similar, indicating that both forms of insight are affected by mood in a relatively similar way (both correlations r=0.18) indicating that both forms of insight are affected by mood to a similar extent. Limited publication bias was identified.

This analysis included papers utilising various depression scales (BDI; PANSS; CDS; HDRS). Although these scales all measure depression, there is the possibility that differences in the focus and structure of depression scales contributes variation to this relationship, for example self-rated measures are qualitatively different in content and structure to researcher/clinician-rated measures. In line with this, a recent review by Mass and Wolf (2012) stated that the strongest correlations with BCIS were obtained with the self-report BDI scale, whereas interview-based assessments of depression such as the HDRS or PANSS scales resulted in weaker associations with the BCIS. This pattern was also seen in our results (table 6.3-1), which may be because self-rated depression scales with explicit responses (BDI and CDS) demonstrate a stronger relationship with the self-rated BCIS scale than clinician/researcher rated scales (HDRS, PANSS), whilst it may also be partly due to the BDI and the BCIS being designed by the same person and therefore sharing a common conceptual basis. While post-hoc analysis indicated that the difference between scales in this study was not significant, future research with a greater numbers of studies is required before firm conclusions can be drawn.

Self-certainty appears to be more independent, at least in relation to mood, but is associated with cognitive abilities (Nair et al., 2014). It has been demonstrated that poor general cognition is related to poor decision-making (Bruine de Bruin, Parker, & Fischhoff, 2007), more specifically the tendency to avoid rational thinking biases (Stanovich & West, 2008). It is therefore suggested that it takes greater cognitive capacity to reconsider one's potentially erroneous beliefs than it does to make a quick decision and stand by it (such as jumping to conclusion bias; Garety et al., 2013). Self-reflection appears to be the more changeable of the two sub-scales as it varies with mood. It is still unclear in which direction these effects work (i.e. does cognition affect SC, or vice versa; does mood affect SR or vice versa), but such a model (see figure 6.4-1) may be useful in furthering the understanding of underlying cognitive mechanisms of both clinical and cognitive insight. The model demonstrates that cognitive insight is associated negatively with both mood and cognitive abilities, but through the different sub-scales, and that it is positively correlated with clinical insight.

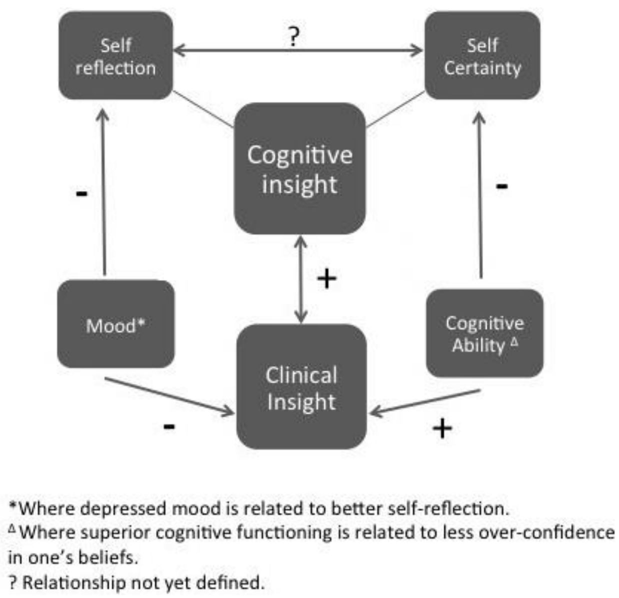


Figure 6.4-1 Theoretical and empirical model of cognitive insight in relation to mood. Lines between cognitive insight and the sub-scales are not arrows because the model is demonstrating how it splits into the two sub-scales.

There have been suggestions that insight can be improved with cognitive-behavioural therapy (as discussed in chapter 3). The model above highlights therapeutic targets by which this could be and are achieved. The relationship between cognitive insight and mood is relevant both clinically and ethically when related to treatment. Whilst clinicians want to improve their patients' understanding of their illness primarily in order to improve compliance with treatment, improving insight may in fact induce depressive symptoms in patients if one subscribes to the defensive denial explanation for this relationship. However if the correct pathways are addressed problems with mood may be bypassed (Misdrahi et al., 2014).

Alternatively therapy could focus on reducing self-certainty, which may improve cognitive insight without inducing low mood, as one would be focussing on reducing cognitive rigidity rather than improving reflectiveness. In contrast, if the depressive realism notion (Haaga & Beck, 1995) were the driving force behind this relationship, then a simplistic interpretation would be that clinicians should ignore patients' mood while attempting to improve insight. A more ethically viable approach to enhancing insight would be to emphasise the positive aspects of insight in terms of acceptance of symptoms and changing one's perceptions and judgements of the world, while also being alert to unwanted changes in mood. Importantly, the work by Kemp and colleagues, as well as Pijnenborg et al., did not find that mood worsened following an intervention to improve insight and compliance, although clearly more research needs to be carried into this issue.

6.4.1 Limitations

The mood-insight relationship, on which all measures in the studies reported here are based, is clearly affected by the nature of self-report, not least self-report in patients with mental illness. Though our analysis indicated that varying depression measures within the literature did not significantly differ in their effect on the strength of the relationship between BCIS and depressive symptoms, it is clear that self-report measures require a certain degree of self-awareness and illness appraisal for patients to accurately rate their depression level and beliefs about themselves and others covered in the BCIS. Additionally, clinical insight measures are usually clinician or researcher rated, albeit scored from patient discourse. The lack of a stronger relationship between the two measures of insight may be explained by the different methods of administering the assessment.

Results of a meta-analysis are dependent on the studies included. Some identified studies were not included due to lack of reporting of specific mood/cognitive insight relationships. It is also acknowledged that that some relevant studies may, unfortunately, have been missed in the literature search. Publication bias analyses were not significant, but cannot be excluded entirely. One problem faced in this particular meta-analysis was that some studies only report data on the sub-scales, or conversely only report the composite index data of the BCIS (see Appendix 1), and as such the total subjects in each analysis was not equal. In general the number and size of studies available for meta-analysis was small so the results must be regarded as awaiting confirmation.

6.4.2 Conclusions

This is the first meta-analysis to investigate the relationship between cognitive insight and mood in patients suffering from psychosis and schizophrenia. The results indicate that there is a small yet significant positive relationship between mood and the BCIS composite index, which is driven by the SR subscale. In contrast, research has shown that self-certainty, but not self-reflectivity, is related to neurocognitive functioning. Nevertheless it appears that both cognitive and clinical insight are influenced to a similar effect size by depression. Such findings provide new avenues to be explored in relation to cognitive-behavioural treatment of psychotic disorders. They also highlight ethical aspects of treating insight, namely that encouraging improved self-reflectiveness may result in patients experiencing lower mood. Studies that examine this longitudinally would be most valuable.

CHAPTER 7

7. RELATIONSHIP BETWEEN METACOGNITIVE EFFICIENCY AND AGE, MOOD, NEUROCOGNITION AND SELF-AWARENESS IN HEALTHY ADULTS

RESULTS FOR HEALTHY ADULTS

This study aimed firstly to investigate metacognitive efficiency and self-awareness in healthy adults over the age of 18 and discover the neurocognitive and demographic correlates of these awareness profiles. This chapter covers the healthy adults' 1) demographic and neurocognitive profile, 2) self-awareness, as measured by the BCIS and DEX, 3) metacognitive efficiency, and 4) whether self-reported self-awareness measures are related to metacognitive efficiency. Each set of measures will be reported as well as their inter-correlation and correlation with age and mood. Basic gender differences will also be reported.

7.1 DEMOGRAPHIC MEASURES

See Table 7.1-1 for overview (means and standard deviations)

A total of 73 healthy adults were recruited into this study, aged 18-88 years (mean 44.5; ± (SD) 21.0), of which there were 42 women (57.8%) with no significant age difference between genders (women 46.97, men 40.9; $t=1.38$, $p=.19$).

		Total Sample	Men	Women
	n	73	31	42
	Age (years)	44.5 (21.0)	40.9 (18.2)	47.2 (22.6)
Mood	**Mood – VAS**	6.79 (1.46)	6.59 (1.52)	6.93 (1.42)
	BDI total (n=73)	5.83 (4.84)	4.45 (3.73)	6.88 (5.34)
	BDI Somatic	3.79 (3.30)	3.00 (2.90)	4.38 (3.49)
	BDI Cognitive	1.67 (1.96)	1.19 (1.22)	2.02 (2.31)
Awareness	**BCIS CI (n=71)**	6.90 (5.36)	7.10 (5.58)	6.73 (5.24)
	BCIS SR (n=71)	19.9 (4.22)	2.47 (3.24)	19.5 (4.80)
	BCIS SC (n=71)	13.0 (3.45)	13.4 (3.45)	12.8 (3.47)
	DEX-sr (n=71)	16.0 (8.01)	16.8 (9.13)	15.4 (7.31)
	DEX-ir (n=41)	10.6 (7.49)	10.4 (6.49)	10.7 (7.78)
	DEX disc (n=41)	-6.95 (8.01)	-9.00 (8.30)	-5.77 (7.72)

Table 7.1-1. Healthy adult mean (standard deviation), age and clinical scores for total sample and by gender.

Ethnicity

61 people (83.6%) in the sample identified as White (British/Irish/European/American); 6 people (8.2%) in the sample identified as Black African/Caribbean; 3 people (4.1%) in the sample identified as Asian; 3 people (4.1%) classed their ethnicity as "Other".

7.2 IQ AND NEUROCOGNITIVE MEASURES

See table 7.2-1 for overview (means and standard deviations).

	Total Sample Mean
Years in Education	14.2 (2.77)
Total WAIS IQ (n=44)	113.4 (15.9)
Trails B-A (n=52)	30.3 (19.3)
Brixton Error (n=30)	12.9 (5.82)
°Memory Recall Total (Time 1) (n=44)	11.3 (3.46)
°Memory Recall Total (Time 2, n=46)	15.1 (8.10)
°Memory Recognition Total (n=46)	25.3 (6.59)
FAS Letters 60s (n=47)	53.7 (15.8)
FAS Letters Error 60s (n=47)	.09 (.282)
FAS Categories 60s (n=47)	70.7 (21.0)
FAS Categories Error 60s (n=47)	.150 (.416)

Table 7.2-1 Healthy adult neurocognitive scores; mean (standard deviation) for total sample (n stated in brackets when ≠ 73; °denotes reporting raw scores, rather than scaled).

Education and IQ

There was a significant negative correlation between age and years in education (r=-.478, p<.001).

There was no significant correlation between Total WAIS IQ and number of years in education (r=.24, p=.11, n=44) and no significant gender difference in total IQ (t=1.91, p=.062). There was no significant correlation between total IQ and average mood (r=-.11, p=.51), BDI scores, BCIS scores (SC, r=.23, p=.14; SR, r=.03, p=.87; CI, r=.12, p=.40) or DEX-sr (r=.13, p=.42).

There was a significant negative correlation between age and total IQ (-.30, p<.05).

Neurocognition

There was no significant correlation between age and any measure of neurocognition (apart from IQ).

7.3 Mood

See table 7.1-1 for overview (means and standard deviations), see table 7.3-1 for correlations.

71 participants completed the BDI questionnaire, 73 completed the mood rating visual analogue scale (VAS). The average mood of the sample was 6.7 (±1.46) out of a possible 10 (where 0 = very sad, 10 = very happy). There was no significant gender difference in average mood (t=-.93, p=.36). The mean sample BDI score was 6.5 out of a possible 63, indicating that on average the sample was psychologically healthy, with only 5 (12% of the total sample) scoring over the cut-off point of 13. Of the participants scoring in the clinical range, 4 were “mild”, 3 were “moderate”. There was a significant gender difference in BDI total score (t=-2.16, p<.05) and BDI cognitive sub scale (t= -1.98, p<.05), with women scoring

significantly higher than men for both (see Table 7.3-1), however this effect was not significant for the BDI somatic sub-scale.

There was a near significant correlation in the expected negative direction between average mood and BDI total (r=-.217, p=.08) and BDI cognitive sub-scale (r=-.31, p<.01), but not the BDI somatic sub-scale (r=-.12, p=.35).

		BDI Total	BDI Somatic	BDI Cognitive
Demographics				
	Age (years, n=72)	-.085	-.066	-.108
	Mood- VAS (n=68)	-.217	-.122	**-.309****
	Years Education (n=73)	-.093	-.131	.025
Neuro-cognition				
	WAIS IQ Total (n=44)	-.018	-.041	.038
	Brixton Error (n=30)	**.495****	**.439***	**.441***
	Trails B-A (n=50)	.220	**.321***	-.033
	Memory Recall (Time 1; n=46)	-.179	-.252	-.015
	Memory Recall (Time 2; n=46)	-.220	-.181	-.154
	Memory Recognition (n=46)	.127	.098	.132
	FAS Letter 60s (n=47)	.066	.033	.098
	FAS Letter Error 60s (n=47)	.260	.176	**.308***
	FAS Category 60s (n=48)	-.029	-.085	.077
	FAS Category Error 60s (n=48)	.096	.075	.095

Table 7.3-1. Correlation coefficients of age, mood and neurocognitive variables (r= Pearson's correlation; p= Significance, 2 tailed where *p<.05, **p<.01; n stated in brackets when ≠73).

7.4 Awareness

See Table 7.1-1 for means see Table 7.4-1 for correlations.

7.4.1 Cognitive Insight (BCIS)

		BCIS CI	BCIS SR	BCIS SC
Demographics	**Age (years)**	-.060	-.203	-.155
	Mood – VAS (n=68)	-.123	-.106	.061
	BDI Total	**.235***	**.366*****	.082
	BDI Somatic	.139	**.282***	.128
	BDI Cognitive	**.324****	**.388*****	-.029
Neuro-cognition	**WAIS IQ Total (n=43)**	.132	.227	.026
	Years Education	.195	**.283****	.044
	Brixton Error (n=29)	.109	.213	.045
	Trails B-A (n=49)	-.022	-.024	-.069
	Memory Recall (Time 1; n=43)	.065	-.012	-.135
	Memory Recall(Time 2; n=45)	.101	.084	-.083
	Memory Recognition (n=45)	.086	-.080	-.061

Table 7.4-1 Correlation coefficients for demographic, mood, clinical and neurocognitive measures with measures of cognitive insight (r=Pearson's correlation; p=significance, 2-tailed*p<.05, **p<.01, ***p<.005; n stated in brackets when ≠73).

Composite Index

The mean CI score was 6.89 (±5.36). There was no significant gender difference in CI scores (t= .28, p=.78). There was no significant relationship between CI and age (r= -.06, p=.62).

There was a positive significant correlation between CI and BDI total score (r=.235, p=.048), however this appeared to be mostly driven by the BDI cognitive subscale (r=.32, p<.01), as the relationship between CI and BDI somatic sub scale was not significant (r=.139, p=.46).

Self-reflectiveness

The mean SR score for this sample was 19.90 (±4.19). There was no significant gender difference in SR score (t=.97, p=.34). There was no significant relationship between SR and age (r=-.20, p=.09). SR scores were significantly related to depression, with a positive correlation between SR and BDI total (r=.37, p<.01); there was also a significant relationship between both BDI subscales and SR (cognitive, r=.39, p=<.001; somatic), r=.28, p=.02). This relationship further supports the results of Chapter 6, in which we demonstrated an overall relationship between SR and depression in patients with schizophrenia.

There was a significant relationship between years in education and SR (r=.28, p<.02) but not WAIS IQ (r=.23, p=.14). There was no significant correlation between SR and any neurocognitive measures (see Table 7.4-1)

Self-certainty

The mean SC score for this sample was 13.01 (±3.45). There was no significant gender difference in SR score. There was no significant relationship between SC and age (r= -.155, p=.197). SC was not significantly correlated with depression or current mood. There was no significant relationship between SC and years in education or WAIS IQ. There was no significant correlation between SC and any measure of neurocognition (see Table 7.4-1).

7.4.2 DEX

See Table 7.1-1 for means and 7.4-2 for correlations.

		DEX-sr	DEX-ir	DEX disc.
Demographics	**Age (years)**	-.161	**-.411****	-.094
	Mood – VAS (n=68)	-.234		
	BDI Total	**.437*****		
	BDI Somatic	**.370***		
	BDI Cognitive	**.404*****		
Neuro-cognition	**WAIS IQ Total (n=43)**	.127	.121	.172
	Years Education	.026	.203	.064
	Brixton Error (n=29)	.115	-.058	-.400
	Trails B-A (n=51)	-.141	-.058	.109
	Memory Recall (Time 1; n=43)	-.058	-.212	.159
	Memory Recall (Time 2; n=43)	.077	**-.372**[a]	-.228
	Memory Recognition (n=43)	.214	.131	-.270

Table 7.4-2. Correlation coefficients for DEX sub-scales, age, mood and neurocognition. Correlations for DEX discrepancy scores and mood have not been reported as the -ir scores were not made on the same day as mood questionnaires. (r=Pearson's correlation; p=significance, 2-tailed; *p<.05, **p<.01, ***p<.005, [a]p<.08; n stated in brackets when ≠ 73).

DEX: Self-rated

71 people completed the self-rated DEX (DEX-sr) questionnaire. The mean DEX-sr score was 16 (±8.01). There was no significant gender difference in DEX-sr scores (t=.71, p=.48) and no significant correlation between DEX-sr and age. DEX-sr scores were significantly related to depression, with a positive correlation with BDI total (r=.44, p<.001), BDI somatic sub-scale (r=.37, p<.01) and BDI cognitive scale (r=.40, p<.001), that is, lower mood was related to lower self-rated executive ability. There was also a near significant negative relationship between current mood (VAS) and DEX-sr (r=-.234, p=.055).

There was no significant relationship between years in education and DEX-sr (r=.03, p=.83) or WAIS IQ (r=.23, p=.14). There was no significant correlation between DEX-sr and any measure neurocognition (see Table 7.4-2).

DEX: Independent-rater

41 relatives or significant others completed the independent-rater DEX questionnaire. The mean DEX-sr score was 10.6 (±7.49). DEX-sr and DEX-ir scores were highly correlated (r-.440, p<.005) indicating that this group of participants had good self-awareness.

DEX-ir demonstrated a significant negative correlation with age (r=-.41, p<.01). There was no significant gender difference in DEX-ir ratings (t=-.12, p=.90). There was no significant correlation between DEX-ir scores and any measure of neurocognition, however there was a negative trend relationship with memory delayed recall (r=-.37, p=.07).

DEX: Discrepancy score

Mean DEX discrepancy score was -6.95 (±8.01). The presence of a negative score indicates that, on average, participants were rating themselves as having worse executive function than their independent-raters (opposite to the pattern seen most commonly in patient groups). Though it appears that men had greater discrepancy scores (men -9.00, 8.30), women -5.77 (7.72) there was no significant gender difference in discrepancy scores (t=-1.25, p=2.18).

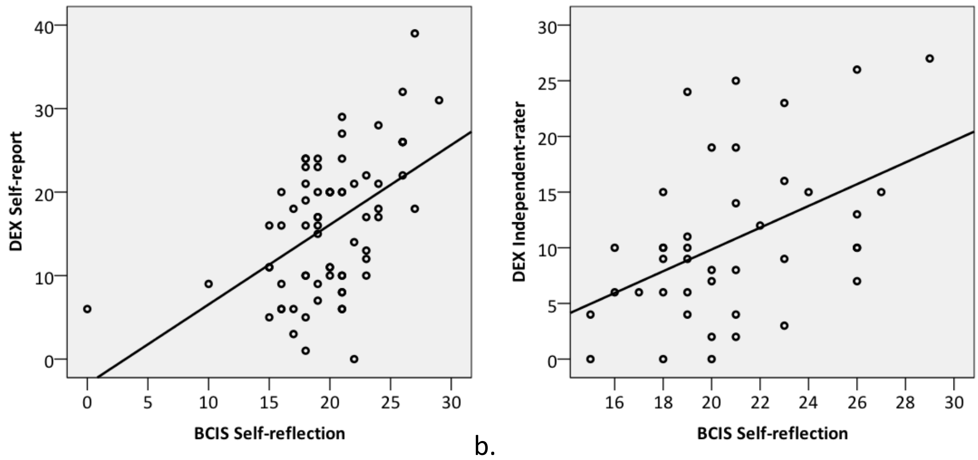
There was no significant correlation between age and the DEX discrepancy score (r=-.09, p=.56). There was no significant correlation between DEX-discrepancy score and any measure of neurocognition (see Table 7.4-2).

7.4.3 *AWARENESS MEASURE CORRELATIONS*

	CI	SR	SC
DEX-sr	**.435****	**.497****	-.067
DEX-ir	**.370***	**.462****	-.155
DEX-discrepancy	-.263[a]	-.221	.233

Table 7.4-3 Correlation coefficients for relationship between awareness measures (BCIS and DEX) (r=Pearson's correlation; p=significance, 2 tailed; *p<.05, **p<.005, [a]p<.10)

There was a significant correlation between BCIS CI and DEX sr scores (r=.44, p<.001), which was driven by the DEX-sr relationship with BCIS SR (r=.50, p=<.001; see figure 7.4-1). There was a significant, positive correlation between DEX-ir and BCIS CI (r=.37, p<.05) that was driven by the BCIS SR (r=.46, p<.005) scores. There was no correlation between BCIS SC score and DEX-sr or DEX-ir scores. There was no significant relationship between DEX-discrepancy score and any cognitive insight score (see Table 7.4-3).



a. b.

Figure 7.4-1 Positive relationship between BCIS SR and a) DEX self-report (r=-.50 p<.001) b) DEX independent-rater (r=.46, p<.005)

7.4.4 METACOGNITION

As stated in Chapter 2, metacognitive efficiency (meta d'/d') was measured in relation to d', which is primary task performance, and meta d' refers to metacognition (i.e. ability to rate oneself as confident when correct and not confident when incorrect), and provides a prediction for the expected value of meta d' given a particular level of task performance. Under the ideal observer model, we would expect meta d' = d', whereby a participant's performance matches their expected performance and therefore meta d'/d' would be expected to = 1.

In this section, the effects of metacognitive efficiency, primary performance and mean confidence will be analysed separately (see Table 7.4-4 for means,7.4-5 for meta d'/d' correlations, and 7.4-6 for d', meta d' and mean confidence).

	Total Sample	**Men**	**Women**
n	53	24	29
Perception meta d'/d'	1.07(.34)	1.11 (.36)	1.05 (.33)
Perception mean confidence	3.79 (.85)	3.87 (.96)	3.72 (.76)
Perception d'	.89 (.16)	.89 (.13)	.90 (.17)
n	37	18	20
Memory meta d'/d'	0.73 (0.81)	0.81 (0.64)	0.65 (0.94)
Memory mean confidence	2.51 (0.56)	2.70 (0.48)	2.34 (0.58)
Memory d'	1.30 (0.56)	1.40 (0.47)	1.21 (0.62)

Table 7.4-4 Mean (SD) metacognitive measures for both perceptual and memory tasks.

		Perception meta d'/d'	Memory meta d'/d'
	Age (years)	**-.380****	-.199
Mood	**Avg. Mood**	.084	.128
	BDI Total	-.091	-.303
	BDI Somatic	-.077	-.171
	BDI Cognitive	**-.263[a]**	**-.415***
Neurocognition	**WAIS IQ Total (n=43)**	.120	.143
	Years Education	.161	.117
	Brixton Error (n=28)	-.233	-.213
	Trails B-A (n=49)	.087	-.183
	Memory Recall (Time 1; n=34)	.113	**.365[a]**
	Memory Recall (Time 2; n=33)	-.083	**.586****
	Memory Recognition (n=33)	-.150	**.367[a]**

Table 7.4-5 Correlation coefficients for relationship between metacognitive efficiency (perception and memory) and clinical, awareness and neurocognitive variables (r= Pearson's correlation; p=significance, 2 tailed; *p<.05, **p<.005, [a]p<.06, [c]p<.08; n stated in brackets when ≠73).

	Age	
	Perception	**Memory**
d'	**-.380***	.016
meta d'	-.171	-.199
Mean confidence	.117	-.275

Table 7.4-6 correlation coefficients for relationship between age and performance (d') and metacognition (meta d'; r= Pearson's correlation; p=significance, 2 tailed; *p<.005) for perception and memory tasks.

Perceptual metacognition

53 participants successfully completed the perceptual metacognition task, after 5 data sets were removed before analysis due to participants scoring lower than 65% correct on the task, which indicated that the staircase procedure (detailed in Chapter 5) had not successfully maintained approximately 70% correct trials in these cases. The mean perceptual metacognitive efficiency (meta d'/d') score was 1.07 (±.34). There was no significant gender difference in perceptual metacognitive efficiency (p=.57), d' (p=.83) or confidence ratings (p=.53; see table 7.4-5).

There was a significant negative correlation between age and perceptual metacognitive efficiency (r=-.38, p<.01; see figure 7.4-2a). There was a significant correlation with age and perception performance (d'; r=.465) but not meta d' (r=-.17, p=.22). There was no significant correlation between either memory task d' (r=.02) or meta d' (r=-.06) and age (see table 7.4-6 and figure 7.4-3).

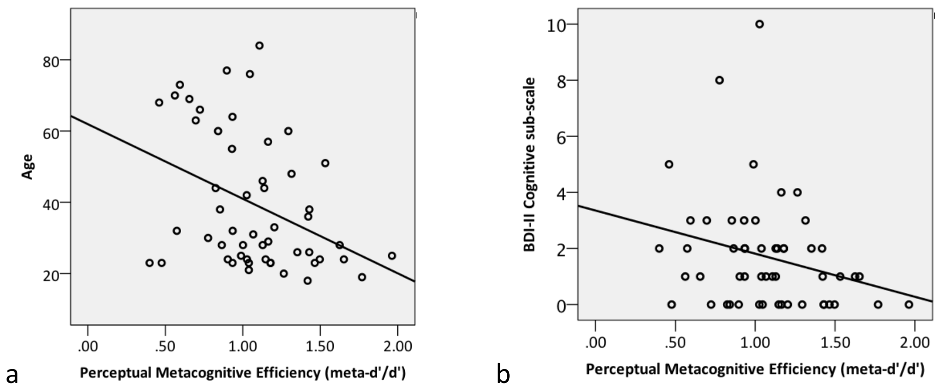


Figure 7.4-2. Negative relationship between a. age and perceptual metacognitive efficiency (r=-.38, p<.01) b. BDI cognitive sub-scale and Perceptual metacognitive efficiency (r=-.27, p=.057)

The negative relationship between perceptual metacognitive efficiency and BDI cognitive sub-scale approached significance (r=-.26, p=.057; see figure 7.4-2b). No other measures of mood or awareness were significantly associated with perceptual metacognitive efficiency, d' or mean confidence rating (see table 7.4-5).

No measures of neurocognition were significantly correlated with perceptual metacognitive efficiency (see table 7.4-5).

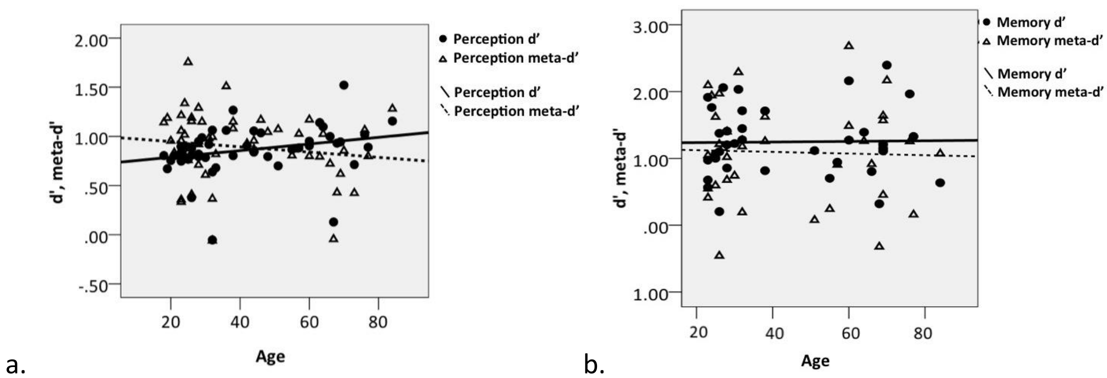


Figure 7.4-3 Shows the relationship between d' and meta d' with age in both a) perceptual and b) memory metacognitive tasks.

Memory Metacognition

38 participants successfully completed the memory metacognition task. Mean memory metacognitive efficiency score (meta d'/d') was 0.72 (0.80). There was a significant gender difference in mean confidence ratings for the memory task ($t=2.13$, $p<.05$) with men rating themselves as more confident (See figure 7.4-4), however there was no gender difference for either metacognitive efficiency ($p=.99$) or task performance (d'; $p=.43$).

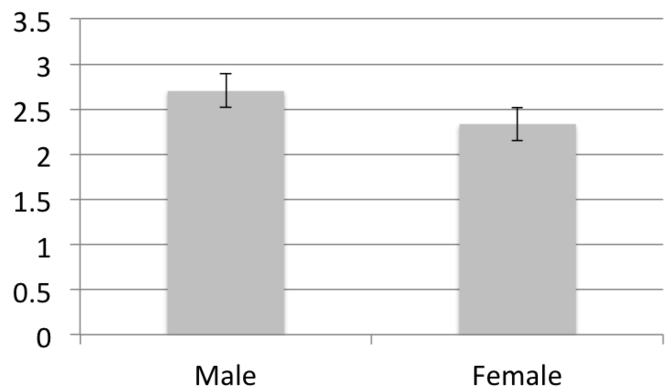


Figure 7.4-4 Shows gender difference in mean confidence on the memory metacognition task

The relationship between age and memory metacognitive efficiency (meta d'/d') was negative but was non-significant ($r = -.199$, $p = .24$). We cannot however draw conclusions regarding a differential effect of age on perceptual compared to memory metacognition as the difference between the domain-specific metacognitive efficiency-age correlations in the subset of subjects who completed both perceptual and memory tasks was itself not significant (Hotelling's $t = 0.66$, $p = 0.51$).

There was a significant negative correlation between memory metacognitive efficiency and BDI cognitive sub-scale ($r=-.42$, $p<.01$); see figure 7.4-5). No other measures of mood or awareness were significantly associated with perceptual metacognitive efficiency, d' or mean confidence rating (see Table 7.4-4).

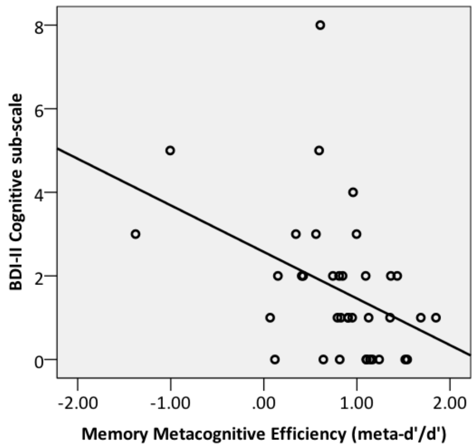


Figure 7.4-5 Shows the negative relationship between BDI Cognitive sub-scale and memory metacognitive efficiency.

There was a number of significant (or near significant) neurocognitive correlates with memory metacognitive efficiency (see table 7.4-5); memory recall from the Wechsler Memory Scale (time 1, r=.37; time 2, r=.59), memory recognition (r=.36).

7.4.5 METACOGNITION AND SELF-AWARENESS

	Perception meta d'/d'	**Memory meta d'/d'**
Perception meta d'/d'	-	**.397***
Memory meta d'/d'	**.397***	-
BCIS CI	-.017	-.242
BCIS SR	.034	-.226
BCIS SC	.068	.173
DEX-sr	.215	.137
DEX-ir	-.051	.228
DEX-discrepancy	-.068	**.480***

Table 7.4-7 Correlation coefficients of relationship between measures of metacognition and measures of insight (r= Pearson's correlation; p=significance, 2 tailed; *p<.05).

Metacognitive dimensions

There was a positive correlation between the two dimensions of metacognitive efficiency (r=.397, p<.05), however, when three memory metacognition outliers were removed (greater than 2 standard deviations beyond the group mean*)* this relationship no longer reached significance (r=.275, p=.150; n=29; see figure 7.4-6).

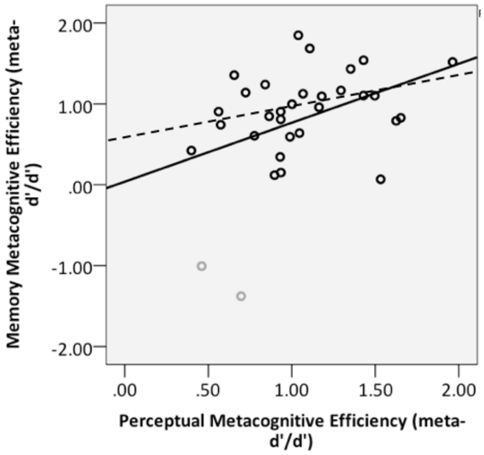


Figure 7.4-6 Shows the positive correlation between perceptual and memory metacognitive efficiency (r=.397; solid trend line), and with outliers (highlighted in gray) are removed (r=.275; dotted trend line).

Cognitive insight

There was no significant direct relationship between either measure of metacognition or any measure of cognitive insight (see Table 7.4-7). Controlling for age had no effect on the relationship with any variable and perceptual metacognitive efficiency, however it did bring the relationship between memory metacognitive efficiency and all BCIS sub-scales to (or approaching) significance (see figure 7.4-7); CI (r=-.518, p=.011) SR (r=-.498, p=.016), SC (r=.405, p=.055).

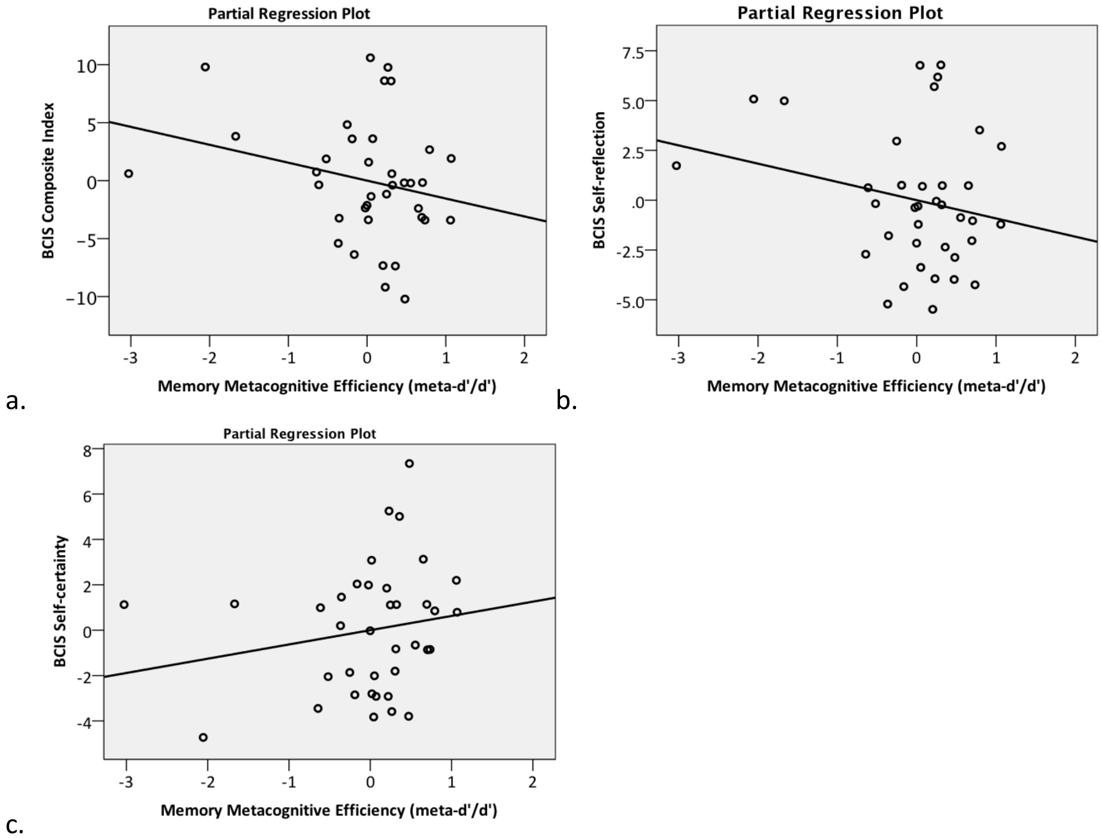
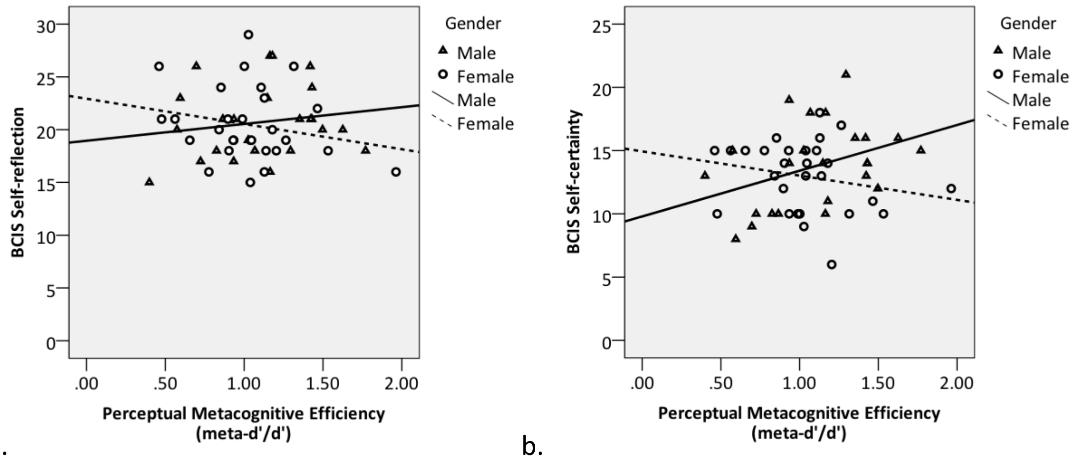


Figure 7.4-7 Partial correlations between memory metacognitive efficiency and a) BCIS composite index b) BCIS SR when controlling for age.

A linear regression was performed predicting perceptual metacognitive efficiency from BCIS subscales, which identified a main effect of gender (t=-3.14, p<.01), and an interaction with SR and SC. (see figure 7.4-8).

The interaction demonstrated that females had a negative relationship between perceptual metacognitive efficiency and SR, whilst males had a positive relationship (t=-2.45, p<.05). Additionally, females demonstrated a positive relationship with SC and perceptual metacognitive efficiency, whereas males demonstrated a negative relationship (t=-2.94, p<.01). This may be explained in terms of men tending to be more overconfident than women, and thus increased SC led to poorer metacognitive function in (see discussion).



a. b.

Figure 7.4-8 Gender interaction with Perceptual metacognitive efficiency and cognitive insight sub-scales a. SR b. SC

The same regression analysis was performed with memory metacognitive efficiency from BCIS sub-scales; there was no main effect of gender (p=.51), SR (p=.26) or SC (p=.74) or interaction between gender and SR (p=.50) or SC (p=.71).

DEX

There was no significant relationship between DEX-sr and either measure of metacognitive efficiency (see Table 7.4-5). However controlling for age brought the relationship between memory metacognitive efficiency and DEX-sr to trend levels (r= -.401, p=.058). There was a significant correlation between memory metacognitive efficiency and DEX-discrepancy (r=.48, p<.02; see figure 7.4-9), which remained significant after controlling for age (r=.47, p=.025; see figure 7.4-10).

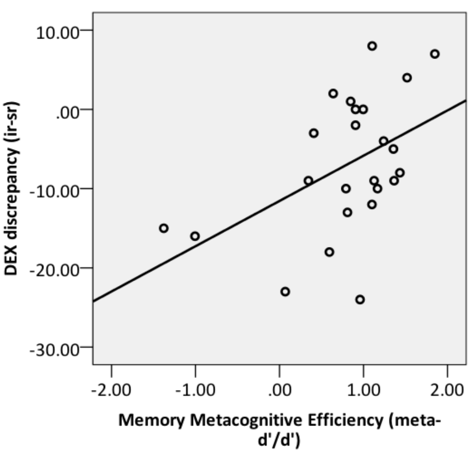


Figure 7.4-9 Correlation between DEX-discrepancy scores and memory metacognitive efficiency.

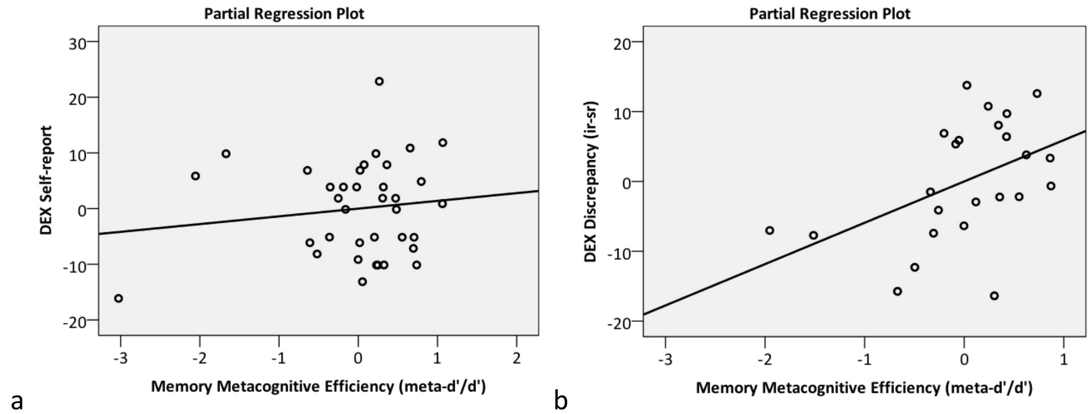


Figure 7.4-10 Partial correlation between memory metacognitive efficiency and a) DEX self-report b) DEX discrepancy, when controlling for age.

There was no significant relationship between memory metacognitive efficiency and DEX-independent, even when controlling for the effect of age.

7.5 Discussion

This study aimed to investigate a group of healthy adults' perceptual and memory metacognitive efficiency as measured on two experimentally controlled computerised assessments and calculated using signal detection theory methods. It also aimed to investigate their self-awareness, as measured on clinical scales suitable for use in the general population. In addition, it aimed to investigate whether experimentally controlled measures of metacognitive efficiency are related to scores on clinical awareness scales, and their neurocognitive correlates. Results are summarised in table 7.5-1.

	Per. m-d'/d'	**Mem. m-d'/d'**	**BCIS - CI**	**- SR**	**- SC**	**DEX - sr**	**DEX -ir**	**DEX -disc**	**BDI total**	**BDI som.**	**BDI cog.**
Perceptual m-d'/d'		+	/	/	/	/	/	/	−ve	/	−ve
Memory m-d'/d'			/	/	/	/	/	+	/	/	−ve
BCIS - CI						+	+	/	+	/	+
- SR						+	+	/	+	+	+
- SC						/	/	/	/	/	/
DEX - sr									+	+	+

Table 7.5-1 Overview of relationship between main variables of interest; + denotes a positive relationship, -ve denotes a negative relationship, / denotes a non-significant relationship.

Effects of Age

The sample had a large age range with no gender differences in this domain. Though the sample was predominantly made up of white participants there was some diversity, with 20% being made up of Black, Asian or "Other" ethnic minority groups. The sample was generally psychologically healthy in that they had low BDI scores, and at the time of assessment were generally happy, with a mean mood of 6.7 out of a possible 10. These two measures of mood were also correlated, indicating that enduring mood (over a two week period, as measured by the BDI) was related to their current mood, and therefore a good representation of general psychological wellbeing. Though there was a decline in IQ as participants' age increased there was no correlation with age on any measure of memory or executive function.

Results supported the hypothesis that "there will be a negative association between metacognitive efficiency and age", however this was only true for perceptual metacognition, meaning that older adults were less efficient about judging their task performance compared to younger adults. A small positive age effect on performance on the perception task was identified. However this was likely due to the adjustment of the task to help older adults with worse visual perception than younger adults, where the contrast between pop-out and non-pop-out Gabor patches was increased. The narrow range of performance levels (between 65-73% correct) in the perceptual task precludes making strong interpretation of changes in d', however, the *relative* values of d' and meta d' can be used to further analyse the data. Results show (figure 7.4-3) that in younger adults, meta d' is similar to or slightly above d' (meta d'/d' ~ 1), whereas in older adults, meta d' drops below d', leading to metacognitive efficiency scores less than expected on an ideal observer model. These results support previous work indicating a weaker association between beliefs and abilities in older adults (Hultsch, MacDonald, Hunter, Levy-Bencheton, & Strauss, 2000; Ross et al., 2012) and age-related differences in the accuracy of confidence judgments (Bender & Raz, 2012; Dodson et al., 2007; Huff et al., 2011; Kelley & Sahakyan, 2003; Pansky et al., 2009; Perrotin et al., 2007; Soderstrom et al., 2012; Souchay et al., 2000, 2007; Toth et al., 2011; Wong et al., 2012). The current results, however, are novel, as previous work did not control effectively for task performance when measuring metacognitive abilities. Controlling for task performance was important in this sample, as it allowed for more accurate assessment of metacognitive performance independent of notable cognitive deficiencies associated with advancing age. Further, these results support suggestions that poor FOK scores may have occurred as a result of poor awareness task performance manifesting as poor task ability (Souchay et al., 2007). Results further the work of Weil et al. (2013), who found that there was an age related improvement in metacognitive efficiency between the ages of 11 and 18, and a non-significant decline between the ages of 20 and 41. Together with results from the current study, there is a suggestion that development of metacognitive efficiency follows a U-shaped curve, where it improves during adolescence, plateaus in early adulthood, and declines as we enter older age.

There was no age effect on memory performance (d’) or metacognition (meta d’); similarly there was a negative but non-significant relationship between metacognitive efficiency and age, which initially suggests that different metacognitive domains are related in a different way to age. However, when post-hoc analyses were carried out to investigate the difference between the two domains of metacognitive efficiency’s relationship with age there was no significant difference between the two. It could therefore be suggested that the lack of significant effect of age on memory metacognition is, in part, related to the smaller sample size in this group compared to that for perceptual metacognition efficiency.

NEUROPSYCHOLOGICAL FUNCTIONING

Results do not support the hypothesis that *"*there will be a positive correlation between executive function and metacognitive efficiency" as there was no significant relationship evident between perceptual metacognitive efficiency and measures of cognition, executive function or memory. This study is the first to investigate the association between experimentally controlled, psychophysical measures of metacognition and executive function, and does not support previous work that awareness, as measured by FOK, is associated with executive function in healthy adults (Souchay et al., 2002). However it does support previous work demonstrating no significant association between IQ and metacognitive efficiency (Weil et al., 2013).

There was a significant positive relationship between memory metacognitive efficiency and all measures of memory. Despite controlling for d' in the calculations of metacognitive efficiency (meta d'/d'), it was not possible to control for memory task performance in the same manner as was possible with the perceptual task, therefore some degree of memory ability is still reflected in the metacognitive efficiency scores. This relationship may also be due to the requirement of memory function for participants to complete the metacognitive task, by recalling current and past memory performance to make accurate ratings.

Results supported the hypothesis that "there will be a positive correlation between the two domains of metacognitive efficiency" as there was an initial significant relationship between the two domains, however when 3 memory metacognition outliers were removed this relationship was no longer significant. It is suggested that this is due to a small sample size who managed to complete both tasks successfully, and that perhaps the full spectrum of metacognitive ability was not represented in this sample. Indeed, if the sample size had been larger it may have become apparent that these points were not truly outliers, but at the lower end of the group scores. Further, other studies investigating the relationship between different metacognitive tasks and domains, found a significant relationship with larger sample sizes (McCurdy et al., 2013; Song et al., 2011).

MOOD AND SELF-REPORTED METACOGNITION

In relation to mood, results did not support the hypothesis that "there will be a positive association between metacognitive efficiency and low mood as measured on …BDI, in both the perceptual and memory domain." In the memory domain, the results in fact identified a significant negative relationship between participants' metacognitive efficiency and BDI cognitive sub-scale scores, indicating that as cognitive symptoms of depression increased, the efficiency of participants' metacognitive judgements decreased. This relationship almost reached significance with perceptual metacognitive ability ($p=.057$). In addition, a significant negative relationship between memory metacognitive efficiency and total BDI score was identified. As metacognitive efficiency was associated with cognitive depression symptoms, as opposed to somatic, it could be suggested that in healthy adults, any sub-clinical cognitive aspects of low mood, such as low-self-esteem, negatively impact on metacognitive judgements. In other words, these results do not support theories suggested in clinical literature that low mood leads to a more "realistic" views of the self. These results are at odds with recent findings suggesting that worry induces more accurate metacognitive judgements in the healthy population (Massoni, 2014), as worry is often a cognitive symptom observed in depression. Indeed, low self-esteem has also previously been associated with better insight into illness (Cooke et al., 2007; Bouvet, Ettaher & Diot, 2010).

Participants' BCIS-SR and DEX-sr scores were correlated, indicating that at least in part the measures assess similar forms of self-awareness. However, results did not initially support the hypothesis that "there will be a significant relationship between metacognitive efficiency and measures of awareness", as there was no direct correlation between participants BCIS scores and either memory or perceptual metacognitive efficiency. However, when controlling for age a significant negative relationship was identified between memory metacognitive efficiency and the BCIS CI and SR scores, and a positive relationship between SC and memory metacognitive efficiency almost reached significance (p=.055). Relationships in this direction were unexpected, as one would assume more self-reflection and less self-certainty would be associated with better metacognitive efficiency. It is therefore suggested that, perhaps in healthy adults, SC scores are not associated with the over-confidence attributed to patients, and thus a greater sense of self-certainty is related to more efficient metacognitive processes and accurate confidence in ones judgements.

The same effect was not evident with perceptual metacognitive efficiency when controlling for age, however a gender interaction was identified between perceptual metacognitive efficiency and both SR and SC sub-scales, where female participants had a positive relationship between perceptual metacognition and both subscales, whereas males demonstrated negative relationship with both sub-scales. This could be explained by the finding that men tend to be more over confident that women, and has been demonstrated in a number of domains, such as exam behaviour (Bessington, Persson, & Willenhag, 2005; Lundeberg, Fox, & Punćcohaŕ, 1994), and business decisions such as stock investment (Barber & Odean, 2001). In the current study results could be interpreted as reflecting an over confidence in men, to the detriment of their metacognitive judgements, but better self-reflection results in better metacognitive efficiency. Women tend to be less over-confident than men (Lundeberg, Fox, & Punćcohaŕ, 1994) and in the healthy population this more accurate self-confidence may be reflected in the positive association between female's BCIS self-certainty and metacognitive efficiency scores. This pattern of results is similar to that seen between BCIS subscales and executive function (as measured by WCST errors) in schizophrenia patients (Kao, Wang, Lu, & Liu, 2011), where it was suggested that this interaction may be due to sex differences in brain structures in healthy adults, over the course of normal development of the frontal lobes, where men have a greater age-related decline in frontal lobe volume compared to women (Cowell et al., 1994; Ingalhalikar et al., 2014). With this in mind it could be suggested that there is a gender interaction relating to frontal lobe function and BCIS scores, as frontal lobe function has been shown to positively correlate significantly with both BCIS (Buchy et al., 2012; Pu et al., 2013) and experimentally controlled metacognitive judgements (Fleming et al., 2010).

There was no significant relationship evident between participants' DEX self-reported scores and metacognitive efficiency in either memory or perceptual domain, suggesting that reported self-awareness of daily functioning is not related to metacognitive efficiency. However, there was a significant positive relationship between the DEX discrepancy score and memory metacognitive efficiency, where a negative DEX discrepancy score (a more objective index, indicative of participants rating their functioning as worse than their independent-rater), was related to poorer memory metacognitive efficiency. This relationship held its significance when controlling for the effect of age. These results were expected, as discrepancy scores have commonly been used as a simple measure of awareness of everyday functioning and memory in clinical studies of anosognosia (Clare et al., 2005). This finding supports work by Harty et al. (2013), who found that error awareness on a computerised task was related to discrepancy scores relating to a number of cognitive domains in a healthy adults sample.

7.5.1 Conclusion

Together, these results suggest that there is a relationship between healthy ageing and a reduction in metacognitive efficiency, which is akin to the reduction in frontal lobe structure and function associated with advanced age. In addition, there is a relationship between efficiency in both domains of metacognition. Further, results demonstrate that low mood, specifically cognitive symptoms of depression, is associated with poor metacognitive efficiency. They also demonstrate that there is a relationship between cognitive insight and memory metacognition, when controlling for age, in healthy adults, however this relationship is not evident with cognitive insight and perceptual metacognition. However, with perceptual metacognition there is a significant association with BCIS sub-scales that is mediated by gender. Finally, there is a relationship between participant-informant discrepancy measures of everyday functioning and memory metacognitive efficiency.

These results contribute to a better understanding of metacognitive efficiency in the healthy population, indicating that different measures placed together under the larger term "metacognition" are, at least in part, related and imply that though the self-report measures of cognitive style and experimentally derived indices were designed to measure different aspects of metacognition, they are associated. Indeed, discrepancy scores may be more strongly associated with objective measures of metacognitive efficiency. It also appears that the two types of metacognitive measure are affected by mood in different ways, indicating that the two types of measure are dissociable in terms of their correlates.

CHAPTER 8

8. RELATIONSHIP BETWEEN METACOGNITIVE EFFICIENCY AND MOOD, NEUROCOGNITION AND SELF-AWARENESS IN FIRST EPISODE PSYCHOSIS

RESULTS FOR FIRST EPISODE PSYCHOSIS PATIENTS

This study aimed to investigate metacognitive efficiency and insight in patients experiencing their first episode of psychosis, who were over the age of 18, and discover the neurocognitive and demographic correlates of these awareness profiles. This chapter covers the FEP patients': 1) demographic and neurocognitive profile, 2) self-awareness, as measured by the BCIS, SAI-E and DEX, 3) metacognitive efficiency, and 4) whether self-report self-awareness measures are related to metacognitive efficiency.

8.1 DEMOGRAPHICS AND CLINICAL RATINGS

See table 8.1-1 for means and standard deviations.

A total of 20 FEP patients were recruited into this study, aged 20-58 years (mean 29.7; ±10.4), of which there were 8 women (40%) with no significant age difference between genders (t=-1.31, p=.207; women 33.7, men 27.5 years). Data were not split by gender due to the low number of participants in each group.

	(n)	Mean scores
	Age (years)	29.7 (10.4)
Mood	**Average Mood – VAS score (13)**	6.06 (2.40)
	BDI total	18.8 (10.6)
	BDI Somatic	12.8 (6.62)
	BDI Cognitive	6.05 (4.56)
Awareness	**BCIS CI**	10.1 (6.36)
	BCIS SR	24.6 (5.34)
	BCIS SC	14.5 (4.92)
	SAI sub-total	15.2 (5.43)
	SAI total	18.1 (5.56)
	DEX-SR	33.3 (13.1)

Table 8.1-1 FEP mean (standard deviation) age and clinical scores for total sample, n stated when ≠ 20.

Ethnicity

13 people (65%) in the sample identified as Black African/British/Caribbean/South-African and 7 people (35%) identified as White British/European.

8.2 IQ AND NEUROCOGNITIVE MEASURES

	Total Sample Mean	Correlation with Age, r
Years in Education (n=19)	12.9 (2.10)	**-.435**[a]
Total WAIS IQ	82.6 (19.4)	-.056
Trails B-A (n=19)	59.6 (39.3)	.240
Brixton Error (n=19)	18.2 (7.20)	-.058
°Memory Recall Total (Time 1; n=19)	17.8 (7.50)	-.185
°Memory Recall Total (Time 2, (n=19)	17.3 (8.85)	.050
°Memory Recognition (n=19)	24.1 (3.68)	-.101
FAS Letters 60s (n=18)	34.1 (13.9)	.037
FAS Categories 60s (n=18)	46.1 (11.9)	-.212

Table 8.2-1 FEP adult neurocognitive scores; mean (standard deviation) for total sample and by gender and correlation coefficients with age (r=Pearson's correlation; p=significance, 2-tailed) where [a]p<.07 (°denotes reporting raw scores, rather than scaled).

Education and IQ

There was a trend correlation between age and years in education (r=-.435, p=.062). There was no significant correlation between Total WAIS IQ and number of years in education (r=.066, p=.789, n=19). There was no significant correlation between age and total IQ or years in education.

Neurocognition

There were no correlations between age and any measure of neurocognition.

8.3 Mood and cognitive function

See table 8.1-1 for means and standard deviations, see table 8.3-1 for correlations.

		BDI Total	BDI Somatic	BDI Cognitive
Demographics				
	Age (years)	.245	.244	.214
	Average Mood- VAS (n=13)	-.491	-.447	-.470
	Years Education (n=19)	.219	.252	.138
Neurocognition				
	WAIS IQ Total	-.305	-.258	-.333
	Brixton Error (n=19)	.162	.147	.163
	Trails B-A (n=19)	**.619****	**.516***	**.684****
	Memory Recall (Time 1; n=19)	-.116	-.154	-.046
	Memory Recall (Time 2; n=19)	.140	.107	.169
	Memory Recognition (n=19)	-.307	-.284	-.299
	FAS Letter 60s (n=19)	-.217	-.124	-.313
	FAS Category 60s (n=18)	-.152	-.075	-.236

Table 8.3-1 Correlations of age, mood and neurocognitive variables (r= Pearson's correlation; p= Significance, 2 tailed) where *p<.05, **p<.01 and 'n' is stated when ≠ 20.

13 FEP patients completed the mood rating VAS and 20 participants completed the BDI questionnaire. The mean average mood of the sample was 6.06 (±2.40) out of a possible 10. The mean sample BDI score was 18.8 out of a possible 63, indicating that on average this group was mildly depressed. There were modest non-significant inverse correlations between average mood VAS score and BDI total (r=-.491, p=.08), BDI somatic sub-scale (r=-.447, p=.13) and BDI cognitive sub-scale (r=-.470, p=.105). All measures of the BDI were positively correlated with the Trails B-A score (total, r=.619, p<.01; somatic, r=.516, p<.05; cognitive, r=.684, p<.01), indicating that worse executive function/processing speed was related to lower mood. There was no relationship between mood and any other measure of neurocognition.

8.4 Awareness

See table 8.1-1 for means and standard deviations see table 8.4-1 for correlations.

8.4.1 *Cognitive Insight (BCIS)*

	BCIS CI	BCIS SR	BCIS SC
Age (years)	**.462***	.265	-.309
Avg. Mood (n=13)	.094	.092	.003
BDI Total	.132	.106	-.056
BDI Somatic	.068	.107	.028
BDI Cognitive	.207	.089	-.170
WAIS IQ Total	.255	.015	-.313
Years Education (n=19)	-.006	.017	.027
Brixton Error (n=19)	-.343	-.075	.367
Trails B-A (n=19)	.141	.295	.138
Memory Recall (Time 1; n=19)	.451	.268	-.299
Memory Recall (Time 2; n=19)	**.451**[a]	.073	**-.512***
Memory Recognition (n=19)	.233	-.090	**-.404***

Table 8.4-1 Correlation coefficients for demographic, mood, clinical and neurocognitive measures with measures of cognitive insight (r=Pearson's correlation; p=significance, 2-tailed) where *p<.05, [a]p<.06.

Composite Index

The average CI score was 10.1 (±6.36). There was a significant relationship between CI and age (r= .462, p<.05). There was no significant relationship between CI and any BDI sub-scale.

There was no significant correlation between CI and years in education or WAIS IQ. There was a relationship of trend significance between CI and memory recall (r=.451, p=.052), however there were no other significant correlations between CI and measures of neurocognition (see table 8.4-1).

Self-reflectiveness

The average SR score for this sample was 24.6 (±5.34). There was no significant relationship between SR and age (r=-.20, p=.09). There was no significant relationship between SR and any BDI sub-scale. This finding is not in keeping with results from Chapter 5, in which an overall small but significant relationship between SR and depression in patients with schizophrenia was demonstrated (r=.018), however this may be related to a smaller sample size in this study and a narrower range of mood scores.

There was no significant correlation between SR and any neurocognitive measures (see table 8.4-1)

Self-certainty

The average SC score for this sample was 14.5 (±4.92). There was no significant relationship between SC and age (r= -.309, p=184). SC was not significantly correlated with and any BDI sub-scale. There was no significant relationship between SC and years in education or WAIS IQ. There were no other significant correlations between SC and measures of neurocognition (see table 8.4-1).

8.4.2 SAI-E

	SAI-E sub-total
Age (years)	-.012
Avg. Mood (n=13)	-.124
BDI Total	-.060
BDI Somatic	-.119
BDI Cognitive	.035
WAIS IQ Total	.412
Years Education	.013
Brixton Error (n=19)	**-.499***
Trails B-A (n=19)	-.174
Memory Recall (Time 1; n=19)	**.687****
Memory Recall (Time 2; n=19)	**.529***
Memory Recognition (n=19)	**.537***

Table 8.4-2 Correlation coefficients for SAI sub-total, age, mood and neurocognition. (r=Pearson's correlation; p=significance, 2-tailed) where *p<.05, ** p<.001; n stated in brackets when ≠20.

SAI-E sub-total

The average SAI sub-total score (not including the medication compliance item) was 15.2 (±5.43). There was no significant relationship between SAI-E sub-total and age, or any measure of mood. There was a significant relationship between SAI-E sub-total and a number of neurocognitive measures, where better function or less errors were related to improved insight; number of errors made on the Brixton test (r=-.499, p<.05); immediate memory recall (r=.689, p<.001), delayed memory recall (r=.529, p<.05); memory recognition (r=.537, p<.05). There was also a trend relationship between SAI sub-total and WAIS total IQ (r=.412, p=.071)

8.4.3 DEX

See table 8.1-1 for overview and table 8.4-3 for correlations. Unfortunately, only 4 DEX-ir responses were received therefore no data will be reported for DEX–ir or discrepancy scores.

	DEX-sr
Age (years)	-.025
Avg. Mood	-.268
BDI Total	**.550***
BDI Somatic	**.479***
BDI Cognitive	**.580****
WAIS IQ Total	-.244
Years Education	.343
Brixton Error	.145
Trails B-A	.324
Memory Recall (Time 1)	.040
Memory Recall (Time 2)	.031
Memory Recognition	-.158

Table 8.4-3 Correlation coefficients for DEX-sr and DEX discrepancy, age, mood and neurocognition. Correlations for DEX discrepancy scores and mood have not been reported as the IR scores were not made on the same day as mood questionnaires (r=Pearson's correlation; p=significance, 2-tailed) *p<.05, **p<.01.

Self-rated DEX score was significantly correlated with all measures mood, whereby lower mood, as identified by cognitive and somatic symptoms, was associated with higher self-reported dysexecutive symptoms (Total, r=.550, p<.05; Somatic, r=.479, p<.05; Cognitive, r=.580, p<.01).

8.4.4 Awareness measure correlations

	CI	SR	SC	SAI-E sub-total
BCIS- CI				**.46***
- SR				**.41**^{b}
-SC				-.15
DEX-sr	.03	.14	.12	0.08

Table 8.4-4 Correlation coefficients for relationship between awareness measures (BCIS and DEX) (r=Pearson's correlation; p=significance, 2 tailed; *p<.05, **p<.01, ^{b}p<.07, ^{d}p<.10)

There was a significant positive correlation between BCIS CI and SAI-E sub-total scores (r=.46, p<.05, see figure 8.4-1), and a trend relationship between total SAI-E score and BCIS CI score (r=.38, p=.0.95) and BCIS SR (r=.41, p=.07). There was no significant relationship between the DEX-sr and any other awareness measures (see table 8.4-4).

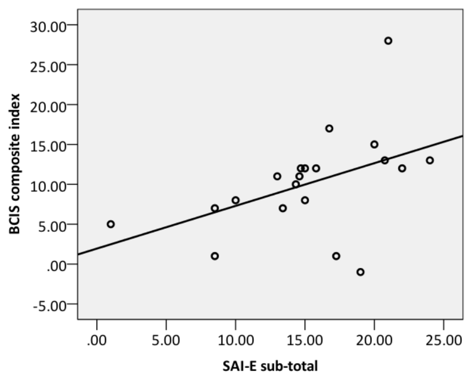


Figure 8.4-1 Scatterplot shows the relationship between two measures of insight, BCIS composite index and the SAI-E sub-total (r=.46, p<.05).

8.5 METACOGNITION

See table 8.5-1 for overview (means and standard deviations) and 8.5-2 for correlations.

	Total Sample	Sample (cases removed)
n	12	6
Perception meta d'/d'	0.89(0.89)	0.87 (0.31)
Perception mean confidence	4.68 (1.09)	4.22 (1.08)
Perception d'	0.63 (0.29)	0.83 (0.11)
n	18	13
Memory meta d'/d'	0.41 (1.22)	0.09 (1.10)
Memory mean confidence	2.19 (1.11)	2.02 (1.11)
Memory d'	0.79 (0.65)	1.06(0.56)

Table 8.5.1 FEP mean (standard deviation) metacognitive measures for both perceptual and memory tasks, means are shown for the total sample and the sample once cases had been removed.

	Perception meta d'/d', n=6	Memory meta d'/d', n=13
Age (years)	-.243	-.417
Avg. Mood	(n=5) .182	(n=7) .551
BDI Total	-.192	-.151
BDI Somatic	-.292	-.055
BDI Cognitive	-.021	-.308
WAIS IQ Total	-.079	.404
Years Education	.249	.435
Brixton Error	-.295	-.449
Trails B-A	-.289	-.750**
Memory Recall (Time 1)	.161	.589 *
Memory Recall (Time 2)	.307	.691 **
Memory Recognition	.172	.756**

Table 8.5-2 Correlation coefficients for relationship between metacognitive efficiency (perception and memory) and clinical, awareness and neurocognitive variables (r= Pearson's correlation; p= significance, 2 tailed) *p<.05, **p<.01, n stated when ≠ 20.

Perceptual metacognition

Out of 12 participants, 7 successfully completed the perceptual metacognition task. 5 data sets were removed before analysis due to participants scoring lower than 65% correct on the task, which indicated that the staircase procedure detailed in Chapter 5 had not successfully maintained approximately 70% correct trials in these cases. The mean perceptual metacognitive efficiency score (meta d'/d') score was therefore 0.87 (±.31). There was no significant relationship between age and perceptual meta d'/d'. Due to the low number of participants successfully completing this task, no firm conclusions can be drawn from this data regarding non-relationships with mood and neurocognitive measures (see Table 8.5-2).

A post-hoc analysis was carried out to determine whether there was a difference between patients who completed the perceptual task successfully and those who did not complete it or scored below 65% responses correct. A significant difference was found between patients who did and did not successfully complete the perceptual metacognition task in measures of executive function; Brixton Error ($t=3.21$, $p<.01$) and Trails B-A score ($t=2.51$, $p<.05$), where those who did complete the task scored significantly lower, and thus had better executive function .

It was also found that those patients who achieved 65% or above in the perceptual task were less confident than the remainder, overall in their performance on the task across trials, to a trend level, and were thus less biased than patients who scored below 65% correct ($t=1.93$, $p=.082$).

Memory Metacognition

Out of 18 participants, 13 successfully completed the memory metacognition task. 5 data sets were removed as their d' was less than 0.25, indicating that they were unable to perform the memory task correctly. The mean memory metacognitive efficiency score (meta d'/d') was therefore was 0.09 (1.10).

There was no significant correlation between age and memory meta d'/d'. There was no significant relationship between memory metacognitive efficiency and mood or neurocognitive measures (see table 8.5-1). There was a significant association between all measures of memory, as well as executive function as measured by trails B-A score, and memory metacognitive efficiency in this clinical group (see figure 8.5-1).

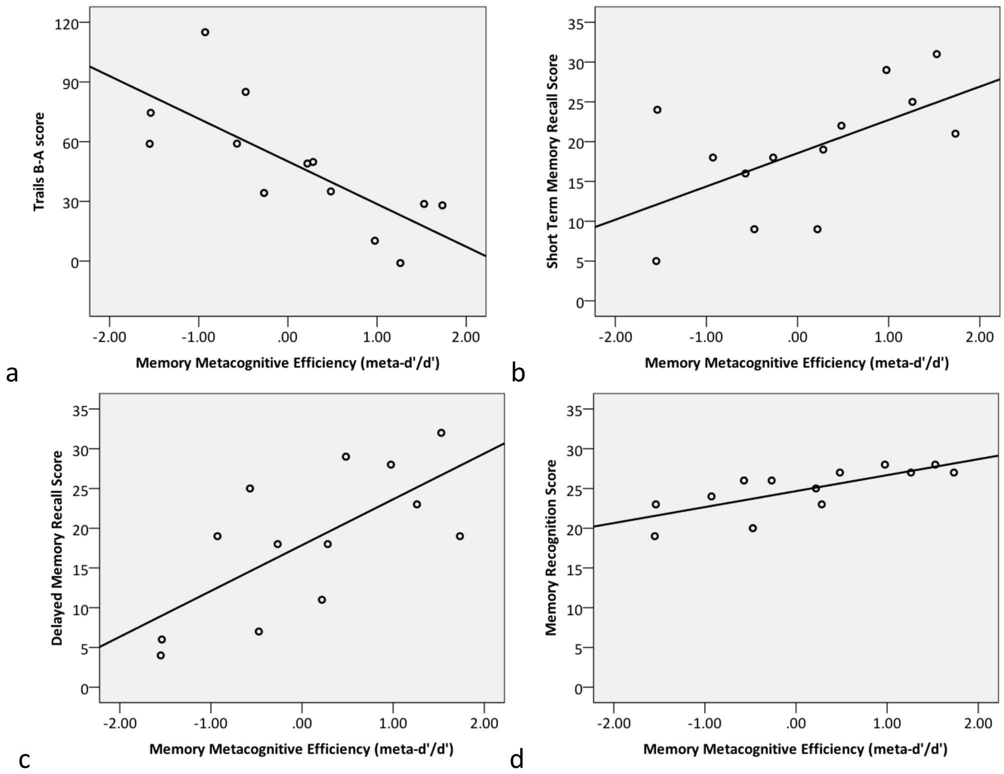


Figure 8.5-1 Scatterplot shows the significant relationship between memory metacognitive ability and a) Trails B-A time (r=-.75, p<.01), b) short term memory recall (r=.59 p<.05) c) Long term memory recall (.69, p<.01) and d) Memory recognition (r=.76, p<.01).

Post-hoc calculations were carried out to investigate whether the unexpected positive association between low mood and poor executive function confounded the lack of any significant association between BDI scores and memory metacognition. However, a partial correlation analysis demonstrated that, even when Trails B-A score was controlled for, there was no significant association between memory metacognitive efficiency and BDI scores (total, p=.34; somatic, p=.157; cognitive, p=.964).

8.5.1 *METACOGNITION AND ILLNESS AWARENESS*

See table 8.5-3 for correlations.

	Perception meta-d'/d' n=6	Memory meta-d'/d' n=13
Perception meta-d'/d'	-	-.052
Memory meta-d'/d'	-.052	-
BCIS CI	.486	-.242
BCIS SR	.475	-.387
BCIS SC	.049	-.144
DEX-sr	-.122	-.023
SAI-E sub-total	.467	.017

Table 8.5-3 Correlation coefficients of measures of metacognition and measures of insight (r=Pearson's correlation; p= significance, 2 tailed, *p<.05, **p<.01).

Metacognitive dimensions

There was no significant correlation between the two dimensions of metacognitive efficiency (p=.891) however this may be due to the small number of participants included (n=6). There were no significant correlations between metacognitive efficiency and any measure of insight.

8.6 DISCUSSION

This study aimed to investigate a group of patients with FEP regarding their metacognitive efficiency as measured on two experimentally controlled computerised assessments and calculated using signal detection theory methods. It also aimed to investigate their self-awareness, as measured on clinical scales. Finally, it aimed to investigate whether measures of metacognitive efficiency are related to scores on clinical awareness scales, and their neurocognitive correlates. Due to the small number of patients who were able to complete the perceptual metacognitive task successfully (n=6), few conclusions can be drawn using these data.

The sample had a mean age of approximately 30 years and about two thirds of the group was from Black ethnic backgrounds, and one third from white ethnic backgrounds, which is in keeping with a higher prevalence of psychotic disorders in ethnic minorities in this catchment area (Fearon et al., 2006). Though mean average mood rating at the time of assessment was 6 out of 10, the mean BDI total score was 18 out of 63, indicating that this patient group was mildly depressed. There was no significant age effect for any measure of neurocognition, possibly due to the small age range of the group.

Though a negative relationship was evident between memory metacognitive efficiency and age, nether measure reached significance; therefore results did not support the hypothesis that "there will be a negative association between metacognitive efficiency and age". However, this may be due to the smaller range in ages in this patient group compared to the healthy controls described in Chapter 7, resulting in an age range too small to produce a significant effect.

Neuropsychological functioning

Results support the hypothesis that "there will be a positive correlation between executive function and metacognitive efficiency" as there was a strong negative correlation between memory metacognitive efficiency and score on the Trails B-A score, thus better executive function was associated with better metacognitive efficiency. This result supports previous work in this patient population that highlighted an association between self-reported measures of metacognition and executive function (Lysaker et al., 2005; Morgan & David, 2010). This also indicates that other domains of metacognition have similar correlates and, though distinct concepts, are possibly associated or mediated by similar cognitive processes. The same relationship was not evident between perceptual metacognitive efficiency and executive function. However, a number of patients were unable to complete the task successfully (i.e. the staircase paradigm was not able to maintain approximately

70% correct responses and FEP participants either failed completely before the full task was complete, or results from a full task were removed). A post-hoc comparison was conducted between those patients who completed the task successfully (i.e. achieved % trials correct greater than or equal to 65%) and those patients who did not. It was found that those who completed the task successfully had significantly better executive function as measured by both number of errors made on the Brixton task, where successful patients had less, and the Trails B-A score, where successful patients had a smaller completion time increase between the two versions of the task. It was also found that patients who were unable to complete the task successfully were more confident in their responses than patients who did complete the task correctly, indicating that they had a stronger “overconfidence” bias. Therefore, despite a lack of significant association between perceptual metacognitive efficiency and executive function, there is some evidence to suggest executive function is related to the amount of bias patients attribute to their metacognitive ratings. As patients with FEP are known to have poor executive function it is therefore suggested that a task with less executive demands is employed to further explore this hypothesis. One such suitable task may be that detailed in Song et al. (2011), where stimuli to be judged on the perceptual task are placed adjacent to one another on a single screen, as opposed to the method used in the current study, where they are presented one after another adding a working memory component.

Results presented here also identified a significant relationship between all three measures of memory performance and memory metacognitive efficiency. Though the meta d’/d’ calculation controls for performance, it is clear that some degree of memory ability is required to adequately perform the memory metacognitive task. Indeed, this result supports the suggestion by Dimaggio & Lysaker, (2010) that poor memory function can result in patients lacking the ability to up-date self-knowledge, and this leads to poor self-awareness. Further, this finding is in keeping with previous work in AD patients by Souchay et al., (2002), which demonstrated that memory metacognitive abilities were more strongly associated with memory in patients, and were more likely to be associated with executive function in healthy adults. Such findings may indicate there is some similarity between awareness profiles and their correlates across neuropsychiatric diagnoses.

Results did not support the hypothesis that "there will be a positive correlation between the two domains of metacognitive efficiency", however this is likely due to the low number of patients who completed the perceptual metacognitive task, and thus the analysis lacked sufficient power.

MOOD AND SELF-REPORTED METACOGNITION

Results did not support the hypothesis that "there will be a positive association between metacognitive efficiency and low mood as measured on the… BDI, in both perceptual and memory domain." Again, this could not be tested adequately for the perceptual task due to low numbers. Regarding memory metacognitive efficiency, results therefore do not support previous work indicating an association between metacognition and mood (Lysaker et al., 2005). However it may be that previous work found an association because measures of both metacognition and mood were self-report questionnaires. Indeed, previous work, including the meta-analysis reported in chapter 6, investigating the relationship between insight and mood has also identified that the strongest associations are between two self-report measures (i.e. shared method variance). The current study utilised novel experimentally controlled, computerised methods of measuring metacognition, whilst also using self-report measures of mood, which may have reduced the degree of association between the two. In the current sample, poor executive function was associated with worse mood, whereas good executive function was associated with better metacognitive efficiency; a post-hoc partial correlation was carried out to confirm whether controlling for executive function would reveal a significant mood/metacognitive efficiency relationship, however the relationship remained non-significant.

Participants' BCIS and SAI-E scores were correlated, indicating that, at least in part the clinical measures assess similar forms of self-awareness, and this is in keeping with previous work regarding the BCIS association with other measures of clinical awareness (Riggs et al., 2012). However, there was no significant association between the DEX and either the BCIS or SAI-E. This may be because the DEX was designed to measure behavioural awareness in dementia rather than schizophrenia.

Results supported previous research regarding mood and clinical insight, demonstrating a significant relationship between DEX-sr and mood, whereby a higher DEX-sr score was associated with lower mood. However this was not evident for either BCIS sub-scale scores, which does not match the results reported in Chapter 6. This may be a result of a lack of power due to the low numbers and limited range of scores.

There was no significant association between any measure of clinical awareness and measures of metacognitive efficiency, which did not support the previous work reported by Lysaker et al. (2005). Instead results support the findings of Morgan and David (2010), who qualitatively analysed verbatim responses on the SAI-E and found that poor metacognitive processing of cognitive experiences did not dictate the awareness patients held regarding their illness, no matter how superficial this awareness may be. Further, as discussed previously, this lack of association may be due to the current measure of metacognition being an experimentally controlled, computerised task, where previous work has used self-report measures. In addition, different measures of insight were utilised in this study (SAI-E, BCIS and DEX; as well as in Morgan and David, 2010) compared to previous work (SUMD; Lysaker et al., 2005) which used an arguably a more cognitively demanding interview measure.

8.6.2 CONCLUSIONS

The main findings of this study are that, in this FEP patient group, there is an association between memory metacognitive efficiency and both executive function and memory performance. The strength of association between perceptual metacognitive efficiency and other relevant measures could not be assessed due to poor completion rates. This in turn appeared to be related to the general cognitive (in particular executive) demands of the task. Further, findings indicated that there was no association between metacognitive efficiency and either mood or measures of insight.

These results add novel findings to the field of metacognition in the FEP population that has, until recently, relied mainly on questionnaire-based assessments of patient awareness. When combined with previous findings it is clear there are neurocognitive correlates shared by both questionnaire and objective, computerised measures of metacognition, indicating they are mediated by the same processes. However, a lack of direct association between awareness measures in this patient group adds further support to the notion that "metacognition" may be too broad a term when referring to various domains of self-awareness assessment in a clinical setting.

Metacognitive training is being developed to improve awareness of illness in patients with FEP (Aghotor, Pfueller, Moritz, Weisbrod, & Roesch-Ely, 2010; Favrod, Maire, Bardy, Pernier, & Bonsack, 2011; Pijnenborg, Van der Gaag, Bockting, Van der Meer, & Aleman, 2011). The findings reported in this chapter indicating that the two forms of metacognition are loosely associated has implications for further development of such training, namely that it must be ensured that training targets the type of self-awareness that requires improvement, rather than general self-awareness as this is a multifaceted concept and impairments vary across domains.

CHAPTER 9

9. RELATIONSHIP BETWEEN METACOGNITIVE EFFICIENCY AND MOOD, NEUROCOGNITION AND SELF-AWARENESS IN EARLY-STAGE DEMENTIA

RESULTS FOR EARLY-STAGE DEMENTIA PATIENTS

This study aimed to investigate metacognitive efficiency and insight in patients with early-stage dementia (ED), and discover the neurocognitive and demographic correlates of these awareness profiles. This chapter covers the ED patients': 1) demographic and neurocognitive profile, 2) self-awareness, as measured by the BCIS, SAI-E and DEX, 3) metacognitive efficiency, and 4) whether self-report self-awareness measures were related to metacognitive efficiency.

9.1 DEMOGRAPHICS AND CLINICAL RATINGS

See table 9.1-1 for overview (means and standard deviations).

A total of 18 patients with early-stage dementia (ED) were recruited into this study, aged 62-93 years (mean 79.6 years; ±9.36), of whom 7 were women (38.9%). There was a difference in age by gender, where men were significantly older ($t=2.93$, $p<.01$; women 72.7, men 84.0 years).

		Total Sample
	(n)	(18)
	Age (years)	79.6 (9.36)
	MMSE	25.9 (2.83)
Mood	**Mood – VAS**	6.87 (1.73)
	BDI total	10.2 (6.21)
	BDI Somatic	7.33 (5.06)
	BDI Cognitive	3.11 (2.29)
Awareness	**BCIS CI**	7.27 (4.98)
	BCIS SR	20.1 (4.51)
	BCIS SC	12.8 (3.24)
	DEX-sr	18.7 (10.9)
	DEX-ir	15.6 (13.7)
	DEX disc (12)	-4.91 (17.2)
	SAI sub-total	8.90 (6.22)
	SAI-E total	10.5 (7.37)

Table 9.1-1 ED mean (standard deviation) age and clinical scores for total sample, where 'n' is stated for values not acquired for all patients.

Ethnicity

16 people (88.9%) in the sample identified as White (British/Irish/European/American); 1 person identified as Black African, 1 person identified as Asian.

Diagnosis

12 of the patients in the sample had a diagnosis of Mild Cognitive Impairment (MCI) and 6 had a diagnosis of Mild Alzheimer's Disease (AD). The mean MMSE score of this group was 25.9 (±2.83).

9.2 IQ and Neurocognitive measures

	Total Sample
MMSE	25.9 (2.83)
Years in Education	13.2 (3.59)
Total WAIS IQ	98.1 (22.96)
Trails B-A	36.0 (65.12)
Brixton Error	25.9 (9.16)
°Memory Recall Total (Time 1)	16.5 (6.28)
°Memory Recall Total (Time 2)	12.3 (8.28)
°Memory Recognition Total	20.2 (6.49)
FAS Letters 60s	38.1 (12.1)
FAS Categories 60s	41.2 (15.5)

Table 9.2-1 ED neurocognitive scores; mean (standard deviation) for total sample. (°denotes reporting raw scores, rather than scaled).

Education and IQ

There was no relationship between age and years in education (r=.14, p=.57) or IQ (r=-.24, p=.34). There was no significant correlation between Total WAIS IQ and number of years in education (r=.25, p=.31).

Neurocognition

There were no correlations between age and any measure of neurocognition.

9.3 Mood

See table 9.1-1 for means and standard deviations.

18 participants completed the mood rating on the visual analogue scale (VAS) and BDI questionnaire. The mean mood of the sample was 6.87 (±1.73) out of a possible 10. The mean sample BDI score was 10.2 out of a possible 63, indicating that on average they were not depressed, however 8 of the 18 patients did score over the clinical cut off of 13. Of the participants scoring in the clinical range, all 8 were “mild”. There was a significant difference in the cognitive and Beck Depression sub-scale somatic scores of this group, where patients endorsed more somatic, or physical, symptoms of depression than cognitive (t=3.73, p<.01).

There was no significant correlation between age, years in education, MMSE or measures of neurocognition and any measure of mood.

9.4 Awareness

See table 9.1-1 for means and standard deviations.

9.4.1 Cognitive Insight (BCIS)

Composite Index

The average CI score was 7.27 (±4.98). There was no significant correlation between CI and any measure of mood or neurocognition.

Self-reflectiveness

The average SR score for this sample was 20.1 (±4.51). There was no significant correlation between SR and any measure of mood or neurocognition.

Self-certainty

The average SC score for this sample was 12.8 (±3.24). There was no significant correlation between SC and any measure of mood. There were no significant correlations between SC and neurocognition.

9.4.2 DEX

Self-rated

The mean self-rated DEX score was 18.72 (±10.9). DEX-sr was significantly, negatively correlated with current mood ($r=-.742$, $p<.05$), but not with any measure of the BDI. There was no significant relationship between DEX-sr and any measure of neurocognition.

Independent rater

DEX-sr and DEX-ir were not correlated (r=-.053, p=.871) indicating that this group of participants had poor self-awareness. DEX-ir demonstrated was not correlated with age or any measure of neurocognition.

Discrepancy score

There was no significant correlation between DEX discrepancy score and age, or any measure of neurocognition.

9.4.3 SAI-E

SAI-E sub-total

There was no significant correlation between SAI-E sub-total and age, mood or neurocognition.

9.4.4 Awareness measure correlations

See table 9.4-1 for correlations.

	-SR	-SC	DEX-sr	-ir	- disc	SAI-E sub-total
BCIS -CI			-.208	-.311	-**.517**[d]	.343
-SR			-.082	-.168	-.355	.115
-SC			.206	.243	.303	-.376
DEX-sr						-.021
-ir						-.156
discrepancy						-.254

Table 9.4-1 Correlation coefficients for relationship between awareness measures (BCIS and DEX) (r=Pearson's correlation; p= significance, 2-tailed; [d]p<.09)

There was a correlation of trend significance between BCIS CI and DEX sr scores (r=-.517, p=.08). However, there were no other significant correlations between awareness measures.

9.5 METACOGNITION

See table 9.5-1 for overview (means and standard deviation) and table 9.5-2 for correlations.

	Mean
N	6
Perception meta d'/d'	1.07 (0.32)
Perception mean confidence	4.39 (0.56)
Perception d'	0.89 (0.16)
N	12
Memory meta d'/d'	0.62 (0.72)
Memory mean confidence	2.19 (0.82)
Memory d'	1.14 (0.39)

Table 9.5-1 Mean (SD) metacognitive measures for both perceptual and memory tasks.

	Perception meta d'/d'	Memory meta d'/d'
Age (years)	.716	-.347
Avg. Mood		(n=7) .555
BDI Total	.327	-.257
BDI Somatic	.106	-.370
BDI Cognitive	.394	.112
MMSE	**.834***	-.054
WAIS IQ Total	.546	.015
Years Education	.211	-.360
Brixton Error	-.608	-.220
Trails B-A	-.082	-.159
Memory Recall (Time 1)	.186	.322
Memory Recall (Time 2)	.139	**.514[a]**
Memory Recognition	.396	.154

Table 9.5-2 Correlation coefficients for perceptual and memory meta d'/d' and age, mood and neurocognition (r= Pearson's correlation; p=significance, 2-tailed; *p<.05, [a]p<.09).

Perceptual metacognition

Out of 7 participants, 6 successfully completed the perceptual metacognition task, 1 data set was removed before analysis due to participants scoring lower than 65% correct on the task, which indicated that the staircase procedure detailed in Chapter 5 had not successfully maintained approximately 70% correct trials in these cases. The mean perceptual metacognitive efficiency score (meta d'/d') score was therefore 1.07 (±.03). There was a significant correlation between MMSE score and perceptual metacognitive efficiency (r=.83, p<.05, see figure 9.5-1). There were no other significant correlations between perceptual metacognitive efficiency and neurocognition, however, due to the low number of participants successfully completing this task, no firm conclusions can be drawn from this data regarding significant or non-relationships with mood and neurocognitive measures (see table 9.5-2).

A post-hoc analysis was carried out to determine whether there was a difference between patients who completed the task successfully and those who did not complete it or scored below 65% responses correct. There was no significant difference between patients who did and did not successfully complete the perceptual metacognition task in measures of executive function; Brixton Error (t=-.717, p=.484) and Trails B-A score (t=.242, p=.812).

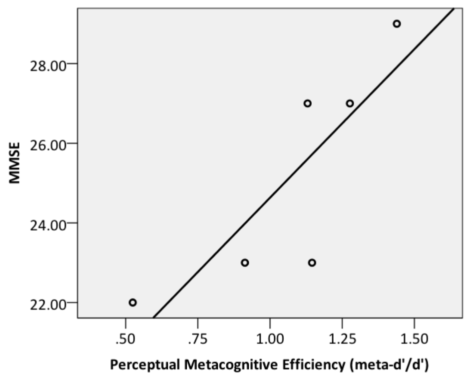


Figure 9.5-1 Scatter plot demonstrates the positive relationship between perceptual metacognitive efficiency (meta d'/d') and MMSE scores (r=.83, p<.05).

Memory Metacognition

Out of 14 participants, 12 successfully completed the memory metacognition task. 2 data sets were removed because their performance on the memory task, represented by d', was less than 0.25. Mean memory metacognitive efficiency score (meta d'/d') was therefore 0.62 (±0.72).

There was no significant correlation between memory metacognitive efficiency and age or mood (see table 9.5-2). There were no other significant correlations between memory metacognitive efficiency and measures of neurocognition.

9.5.1 *METACOGNITION AND ILLNESS AWARENESS*

	Perception meta d'/d'	**Memory meta d'/d'**
BCIS CI	.590	.456
BCIS SR	**.819***	.309
BCIS SC	-.124	-.340
DEX-sr	-.401	-.178
DEX-ir	-	**-.678***
DEX-discrepancy	-	-.377
SAI-E sub-total	-.049	.255

Table 9.5-3 Correlation coefficients of measures of metacognition and measures of insight; correlation between memory and perceptual metacognitive efficiency scores could not be performed due to the low n (=5) (r=Pearson's correlation; p= significance,2 tailed;*p<.05).

There was a significant correlation between perceptual metacognitive ability and BCIS SR (r=.819, p<.05, see figure 9.5-3) however due to the low n (=6) caution should be drawn when interpreting these results.

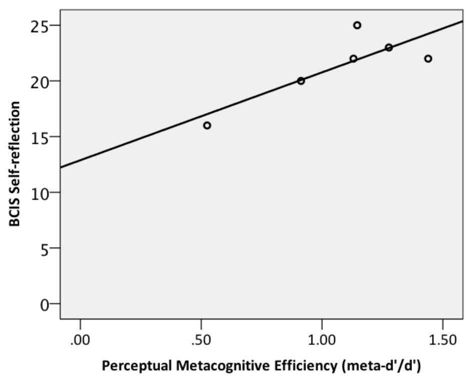


Figure 9.5-2 Scatter plot demonstrates the relationship between perceptual metacognitive efficiency (meta d'/d') and BCIS sr score (r=.82, p<.05).

There was a significant negative correlation between DEX-ir and memory metacognitive efficiency (r=-.678, p<.05).

9.6 DISCUSSION

This study aimed to investigate a group of patients with ED regarding their metacognitive efficiency as measured on two experimentally controlled computerised assessments and calculated using signal detection theory methods. It also aimed to investigate their self-awareness, as measured on clinical scales. Finally, it aimed to investigate whether measures of metacognitive efficiency are related to scores on clinical awareness scales, and their neurocognitive correlates.

Analysis of demographic measures demonstrates that the sample had a mean age of approximately 80 years old. The majority (16) of patients were from a white ethnic background, with one patient identifying as Indian and one identifying as Black African.

Mean average mood rating at the time of assessment was 6.8 out of 10 and the mean BDI total score was 10 out of 63, indicating that this patient group was, on average, not depressed, though 8 patients rated themselves in the “mildly” depressed. There was also a significant effect of Age on MMSE scores, indicating that, in this sample, younger patients had more cognitive deficiencies. This may be due to adults at the younger end of the elderly population presenting to services more often with severe memory complaints than older adults.

Results did not support the hypothesis that “there will be a negative association between metacognitive efficiency and age”. However, this may be due to the smaller range in ages in this patient group compared to the healthy control group described in chapter 7. Indeed, a lack of age effect was also observed in the FEP group, which also had a smaller range of ages included in their sample.

NEUROPSYCHOLOGICAL FUNCTIONING

Results did not directly support the hypothesis that “there will be a positive correlation between measures of executive function and metacognitive efficiency” as there was no correlation between either perceptual or memory metacognitive efficiency and number of errors made on the Brixton task or Trails B-A score, making them at odds with previous clinical findings (Lopez et al.,1994; Michon et al., 1994). Neither was there a significant relationship between both measures and memory scores, contrary to previous findings (Souchay et al., 2002; Gilleen, Greenwood & David, 2014) that have indicated a more significant association exists between metacognition and memory function in patients, whereas healthy adults demonstrated a stronger association between metacognition and executive function. However, perceptual metacognitive efficiency was positively and significantly associated with MMSE scores, indicating that as general cognitive ability declined, so did metacognitive efficiency, akin to previous clinical findings (Chen et al., 2014; Zanetti et al., 1999). It should be noted that, due to the low numbers in this analysis, interpretations of these results should be made with extreme caution. Only 6 patients successfully completed the perceptual task, and it was identified that some patients' visual perceptual abilities were too poor, even after adjusting the starting contrast between the two stimuli and the duration of stimuli presentation. It is suggested that an easier task is employed, such as that detailed in (Song et al., 2011), where stimuli to be judged on the perceptual task are placed adjacent to one another on a single screen, as opposed to the method used in the current study, where they are presented one after another.

Results did not support the hypothesis that "there will be a positive correlation between the two domains on metacognitive efficiency", however this could not be adequately tested due to the low number of patients who completed the perceptual metacognitive task.

Mood and self-reported metacognition

Results did not support the hypothesis that "there will be a positive association between metacognitive efficiency and low mood as measured on the …BDI, in both the perceptual and memory domain", and there was no relationship between metacognitive efficiency and either BDI scores or current mood, as measured on the VAS. These results do not support previous work in this domain that has indicated there is an association between low mood and awareness of memory deficits (Chen et al., 2014; Aalten et al., 2005).

However, this may be due to the lack of cognitive symptoms observed in this participant group. ED patients reported significantly more somatic symptoms compared to cognitive symptoms of depression in this group; in chapter 7 it was suggested that there is more of an association between cognitive symptoms of depression and metacognitive efficiency, compared to somatic symptoms. This pattern of results may explain the non-significant results reported in this chapter. Again, low completion rates on the perceptual metacognitive task precluded an adequate test of this hypothesis.

Participants' clinical awareness scores were not correlated with each other. This is likely because two assessments utilised in this study were initially designed for completion by or with patients with psychosis (SAI-E and BCIS) therefore some questions may not directly translate to experiences of patients with dementia. Additionally one questionnaire was designed to identify awareness of Dysexecutive syndrome (DEX). However, leaving aside the problems with capturing different domains of awareness using the available standardised scales, this result may have come about because different aspects of self-awareness are not associated in this patient group. Finally, results indicated that mood was not related to any measure of insight in this group of elderly people displaying an overall low number of depressive symptoms, perhaps due to the higher reporting of somatic versus cognitive symptoms of depression in this group.

It was not possible to adequately test the hypothesis that "there will be a significant relationship between metacognitive efficiency and measures of awareness", due to the recruitment of a lower than intended number so participants. However, an exploration of the data did appear to show a significant positive relationship between perceptual metacognitive efficiency and BCIS SR. The relationship with self-reflection was in the expected positive direction, meaning that as self-reflectiveness improved, so did metacognitive efficiency. As with other results relating to perceptual metacognitive efficiency, final analyses only involved 6 data sets and so results should be interpreted with caution and are for illustrative purposes only.

Other limitations include the effect of medication; due to the small number of participants completing assessments this could not be included. We also only included patients who had relatively high MMSE scores, and thus were in the early stages of dementia. These findings can therefore not necessarily be applied to patients with later stage dementia, and would be useful research to pursue in the future.

9.6.1 Conclusions

The findings of this preliminary study are that, in this ED patient group, there is an apparent association between perceptual metacognitive efficiency and both general cognitive function, as measured on the MMSE, and cognitive insight, as measured on the BCIS. A lack of association between clinical questionnaire measures and objective task measures of self-awareness indicates that these measures assess behaviourally distinct concepts, and thus the term "metacognition" may be too broad in a clinical setting without adding further information to the context in which it is being used.

There was an issue with this group in successfully completing the perceptual metacognitive task. This related to either patient's inability to see or distinguish between the stimuli presented, or the staircase paradigm being unable to maintain approximately 70% correct total responses, where the n was 6 compared to 14 in the memory task where there was no staircase paradigm to control for performance effects. A lack of staircase paradigm controlling for performance within the memory task may explain the lack of an association between these measures and memory metacognitive efficiency, as memory ability may be confounding the association. Studies with more appropriately tailored stimuli for use in elderly and impaired populations plus a larger number of participants would be necessary to confirm these suggestions, such as Song et al. (2011).

CHAPTER 10

10. COMPARISON OF SELF-AWARENESS AND METACOGNITIVE EFFICIENCY BETWEEN HEALTHY AND CLINICAL POPULATIONS

RESULTS FOR BETWEEN-GROUP COMPARISONS

This chapter aimed to compare 1) healthy adults under the age of 60 years, first episode psychosis (FEP) patients and depressed patients, 2) healthy adults of 60 years and older and patients with early-stage dementia (ED), and 3) ED and FEP patients (whilst acknowledging the difference in age), on measures of awareness and metacognition. Due to the small number of patients who completed the perceptual metacognitive task, these data were not included in the current analyses.

10.1 DEMOGRAPHICS

	Controls (<60 years)	Controls (>60 years)	Depressed	FEP	ED
Age (years)	32.0 (10.5)	71.7 (8.2)	26.8 (7.46)	29.7 (10.4)	79.6 (9.36)
Gender (% fem.)	54	65.2	66.7	35	38
Years Education	15.1 (1.99)	12.2 (3.2)	16.1 (2.92)	12.9 (2.11)	13.2 (3.59)
BDI total	5.96 (4.46)	5.57 (5.66)	32.7 (11.1)	18.8 (10.6)	10.3 (6.22)
BDI somatic	4.26 (3.34)	4.09 (4.08)	21.5 (7.05)	12.8 (6.62)	7.33 (5.06)
BDI cognitive	1.78 (2.02)	1.48 (1.86)	11.2 (4.54)	6.05 (4.56)	3.11 (2.30)

Table 10.1-1 Mean (standard deviation) demographic and mood scores for each participant group.

10.1.1 YOUNGER ADULTS, PATIENTS WITH FEP AND DEPRESSED PATIENTS

There was no significant difference in age between younger healthy adults, FEP patients and patients with depression. The FEP group had spent significantly fewer years in education than the other two groups, and there was no significant difference between the healthy and depressed group. There was a significant difference between all three groups in all BDI measures of depression (total, F=74.8, p<.001; somatic, F= 74.0, p<.001; cognitive, F= 50.9, p<.001) where HC<FEP<depressed for all three scores.

10.1.2 Older adults and ED

There was a significant difference in age between older healthy adults and patients with ED (t=-2.88, p<.01); the patient group was significantly older than the healthy control group with a mean difference of 7.9 years, where the mean age of the healthy adult group was 71.7 years and the ED group was 79.6 years. There was no significant difference between groups in the number of years spent in education. The ED group was significantly more depressed than the healthy older adults in all BDI measures (total, t=2.53, p<.05; somatic, t=2.28, p<.05; cognitive, t=2.52, p<.05). The groups were further compared on their executive function and memory abilities to ensure that healthy older adults were not suffering from undiagnosed mild cognitive impairment; healthy older adults made significantly less errors on the Brixton task (t=3.90, p<.001) and performed significantly better on the Wechsler Memory Scale (WMS; raw score) recall items (short term, t=7.06, p<.001; long term, t=4.98, p<.001) than the ED group.

10.1.3 FEP and ED

There was no significant difference between the FEP and ED group in the number of years spent in education, however the FEP group were significantly more depressed, as indicated by all BDI measures (total, t=2.99, p<.01; somatic, t=2.81, p<.01; cognitive, t=2.55, p<.05).

10.2 INSIGHT

Measure of insight	Controls (<60 years)	Controls (>60 years)	Depressed	FEP	ED
n	50	23	15	20	18
BCIS CI	7.48 (5.33)	6.39 (5.89)	13.8 (4.07)	10.1 (6.36)	7.28 (4.98)
BCIS SR	20.5 (3.52)	19.0 (5.52)	37.7 (4.79)	24.6 (5.34)	20.1 (4.51)
BCIS SC	13.0 (2.91)	12.7 (4.48)	23.9 (4.13)	14.5 (4.92)	12.8 (3.24)
DEX-sr	17.7 (8.22)	14.0 (6.93)	39.5 (16.7)	33.3 (13.1)	18.7 (10.9)
DEX-ir	-	6.92 (4.05)	-	-	15.5 (13.7)
DEX disc	-	-6.23 (5.70)	-	-	-4.92 (17.2)
SAI 1-8	-	-	-	13.0 (4.67)	8.61 (5.63)
SAI-E sub-total	-	-	-	15.2 (5.43)	8.84 (6.04)

Table 10.2-1 Mean scores and standard deviations for clinical insight scales in each participant group. (- denotes data not used in this analysis).

10.2.1 YOUNGER ADULTS, PATIENTS WITH FEP AND DEPRESSED PATIENTS

For overview of means and standard deviations see table 10.2-1, for between group comparisons see table 10.2-2.

Measure of insight	F-value	Group differences
BCIS CI	8.24*	FEP=HC<Dep
BCIS SR	95.2*	HC<FEP<Dep
BCIS SC	51.1*	FEP=HC<Dep
DEX-sr	27.8*	HC<FEP=DEP

Table 10.2-2 One-Way ANOVA to compare FEP, Depressed and healthy control groups (F-value=ANOVA comparison of means; *p<.001). Group difference calculated using Scheffé's post-hoc tests.

Results demonstrated that there were significant group differences between all measures of the BCIS (CI, F=8.24,p<.001; SR, F=95.2,p<.001; SC, F=51.1, p<.001; see table 10.2-2; see figure 10.1-1a,b,c) .There were also significant group differences on the DEX self-rated score (DEX-sr, F=.27.8, p<.001; see figure 10.1-1d) where HC<FEP=Dep (higher scores = more difficulties). Only 4 independent raters returned the questionnaires from the FEP and depressed groups so analyses could not be carried out using these scores.

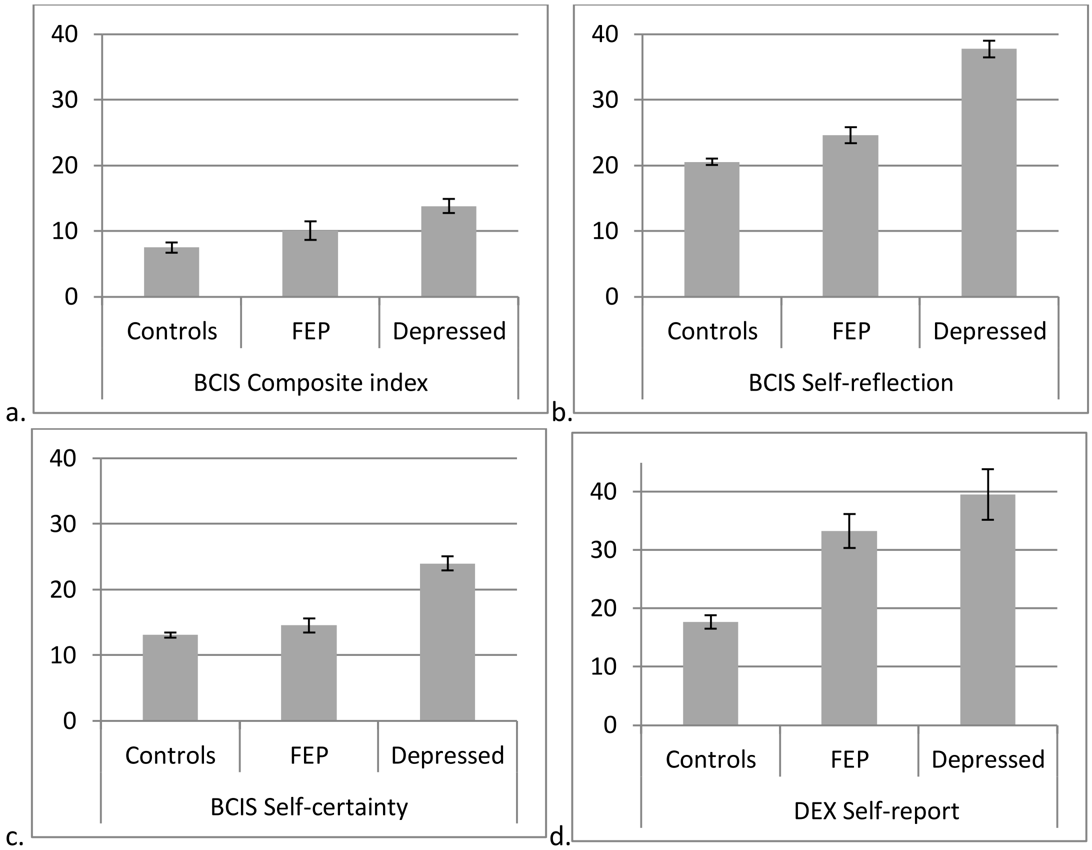


Figure 10.2-1 Bar charts illustrating the significant difference between healthy adults<60, FEP and depressed groups in a. BCIS composite index, b. BCIS SR, c. BCIS SC, d. DEX self-report. Error bars represent standard error. Healthy adults n=50; FEP n= 20, Depressed n=15.

10.2.2 OLDER ADULTS AND ED

For overview of means and standard deviations see table 10.2-1, for between group comparisons see table 10.2-3.

Measure of insight	t-value	Mean difference
BCIS CI	-.511	.886
BCIS SR	-.665	1.61
BCIS SC	-.144	.181
DEX-sr	-.170	4.77
DEX-ir	-2.18[a]	8.66
DEX discrepancy	.-261	1.31

Table 10.2-3 t-values for difference between means of patients with ED/dementia and older healthy controls (age>=60) (t= t-test for equality of means; p= Significance, 2 tailed where [a] p<.06, *p<.05)

There was no significant difference between the patients and control participants in any BCIS sub-scale. There was no significant difference between DEX self-report and discrepancy scores, however there was a difference that almost reached significance in DEX independent rater scores (t= -2.18, p=.056; see figure 10.2-2).

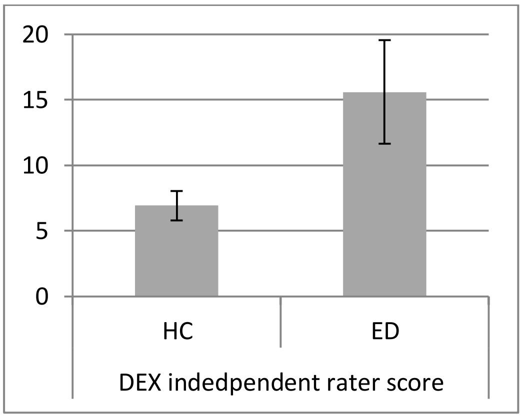


Figure 10.2-2 Bar chart illustrating the difference between DEX independent rater scores for healthy older adults and early dementia patients (p=.056). Error bars represent standard error. Healthy adults n= 23, ED n = 18.

10.2.3 FEP AND ED

For overview of means and standard deviations see table 10.2-1, for between group comparisons see table 10.2-4.

Clinical awareness scores were compared across the patient groups of interest; FEP and ED, to investigate potential differences in their awareness profiles. Many of the ED patients were confused by the final question on the SAI-E "How do you feel when people do not believe you?" therefore a total was calculated removing this from both groups' final scores (SAI 1-8). In addition, the SAI-E total was not included in this analysis as it was not analysed or reported in the ED group (chapter 9) due to the small number of patients taking or offered medication relating to memory difficulties.

Measure of insight	t-value	Mean difference
BCIS CI	1.51	2.82
BCIS SR	2.78**	4.49
BCIS SC	1.22	1.67
DEX-sr	3.69***	14.5
SAI-E 1-8	2.61*	4.37

Table 10.2-4 t-values for difference between means of patients with FEP and early stage (t= t-test for equality of means; p= Significance, 2 tailed where [a] p<.06, *p<.05, **p<.01, ***p<.001)

There were significant differences between BCIS SR scores (t=2.78, p<.01, see figure 10.2-3a) and DEX self-rated scores (t-3.69, p<.001, see figure 10.2-3b), with the FEP group scoring significantly higher in SR scores. The FEP group also had higher self-report DEX scores, despite the ED group making significantly more errors on the Brixton task (t=-2.86, p<.01), and therefore having worse executive function. Post-hoc analyses indicated that this might be related to the higher reported levels of depression in the FEP group (BDI total, t=2.99, p<.005; BDI somatic, t=2.81, p<.01; BDI cognitive, t=2.456, p<.05).

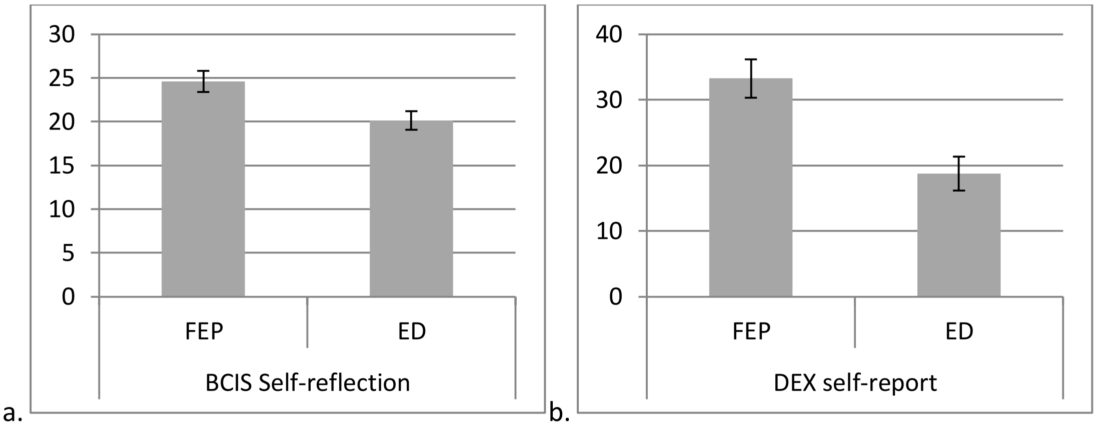


Figure 10.2-3 Bar charts illustrating the significant difference between FEP and ED patient groups in a. BCIS SR, b. DEX self-report. Error bars represent standard error. FEP n= 20, ED = 18.

There were significant differences between FEP and ED patients in their scores on the SAI-E (t=2.61, p<.05; see figure 10.2-4) based on scores generated from items 1-8.

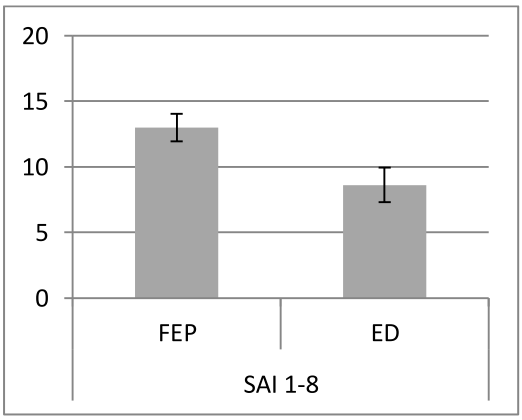


Figure 10.2-4 Bar charts illustrating the difference between FEP and ED patient groups in SAI 1-8 scores, Error bars represent standard error.

10.3 METACOGNITION

Measure of Metacognition	Controls (<60 years)	Controls (>60 years)	Depressed	FEP	ED
n	24	23	13	13	13
Memory meta d'/d'	0.89 (0.43)	0.66 (0.92)	1.04 (0.57)	0.09 (1.09)	0.63 (0.72)
Memory d'	1.30 (0.47)	1.39 (0.65)	1.10 (0.61)	1.06 (0.56)	1.14 (0.39)
Memory confidence	2.60 (0.47)	2.39 (0.68)	2.79 (0.59)	2.01 (0.59)	2.19 (0.82)

Table 10.3-1. Mean standard deviations scores for memory metacognitive efficiency values in all participant groups

10.3.1 YOUNGER ADULTS, PATIENTS WITH FEP AND DEPRESSED PATIENTS

For overview of means and standard deviations see table 10.3-1, for between group comparisons see table 10.3-2.

Measure	F-value	Group difference
Meta d'/d'	7.53**	FEP<HC=Dep
d'	1.52	HC=FEP=Dep
Mean confidence	4.33*	FEP<HC=Dep

Table 10.3-2. Mean difference in memory metacognitive efficiency between healthy younger adults, FEP patients and depressed patients (F-value=ANOVA comparison of means; p= Significance, 2 tailed where *p<.01, **p<.001). Group difference calculated using Scheffé's post-hoc tests.

There was a significant difference between healthy younger controls, FEP patients and patients with depression in memory metacognitive efficiency (F=7.53, p<.001), with Scheffé's post-hoc tests demonstrating that FEP<HC=Dep. There was also a significant difference in confidence ratings (F=4.33, p<=.01), where FEP<HC=Dep (see figure 10.3-1), despite no significant difference in task performance, as measured by d'. Figure 10.3-1a illustrates that both depression and healthy groups' metacognitive efficiency is close to matching the ideal observer model (where meta d'/d' = 1), whereas FEP patients have a much lower mean score of 0.09. Further, 10.3-1b illustrates that FEP patients had the least confidence bias, and both healthy adults and depressed patients had comparable bias towards over confidence.

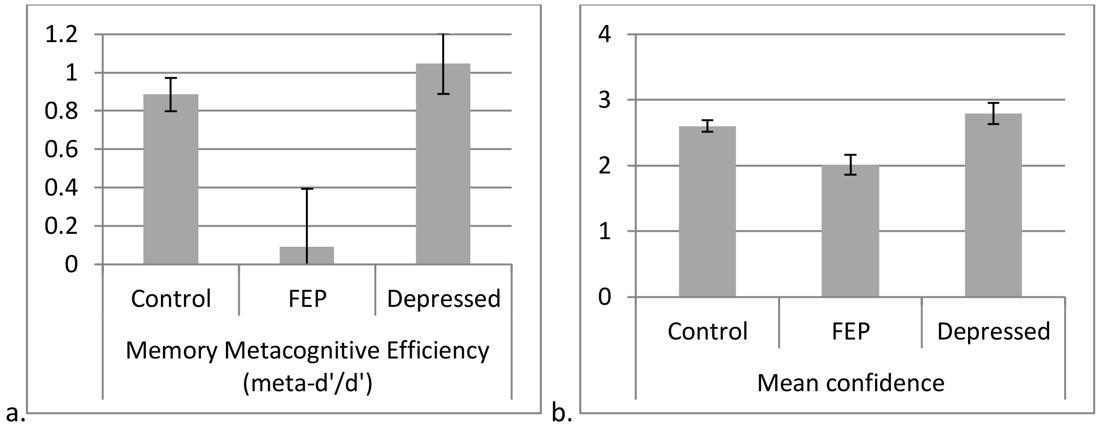


Figure 10.3-1 Bar chart illustrating the difference between healthy controls<60, FEP and depressed groups in memory metacognitive efficiency (meta d'/d'). Error bars represent standard error.

10.3.2 Older adults and ED

For overview of means (standard deviations) see table 10.3-1, for between group comparisons see table 10.3-3.

Measure	t-value	Mean difference
Meta d'/d'	0.18	0.07
d'	1.80	0.41
Mean confidence	0.05	0.02

Table 10.3.3. Shows the mean difference in memory metacognitive efficiency between healthy older adults and those with ED (t-value= t-test for equality of means; p= Significance, 2 tailed where *p<.05, **p<.01)

There were no significant differences between older adults and ED patients regarding memory metacognitive efficiency, d' or confidence (see table 10.3-3).

10.3.3 FEP and ED

Domain	Measure	t-value	Mean difference
Memory	**Meta d'/d'**	-1.44	-0.53
	d'	-0.38	-0.07
	Mean confidence	-0.47	-0.18

Table 10.3-4. Shows the mean difference in perceptual and memory metacognitive efficiency patients with FEP and those with ED (t-value= t-test for equality of means; p= Significance, 2 tailed where *p<.05, **p<.01)

There was no significant difference between clinical groups in their memory metacognitive efficiency, memory performance or task confidence.

10.4 Discussion

This study aimed to investigate the difference between healthy adults and clinical groups regarding their insight on a number of clinical self-awareness scales, and metacognitive efficiency across two domains. Though there were small numbers of patients included in this study, the comparisons are a useful pilot investigation into the potential differences between groups.

There was no significant difference in the ages of healthy younger adults, patients with depression and patients with FEP. FEP patients had spent fewer years in education than the healthy and depressed groups. In relation to mood, the healthy group had the lowest depression scores on all measures, with FEP scoring higher than healthy adults but lower than depressed patients. In contrast, the patients with ED were significantly older on average than the healthy older adult group but had spent a similar number of years in education. The ED group was significantly more depressed than the healthy older adults.

There was a significant difference in all clinical measures of self-awareness between healthy younger adults (<60 years old), patients with depression and patients with FEP. Patients with depression scored significantly higher than the other groups on the SR sub-scale, and thus had a higher CI score, despite having the highest SC scores. This pattern of results suggests that persons with depression are more likely to reflect on their self-beliefs, but may be more certain of their conclusions as a consequence. FEP patients scored significantly lower than depressed patients on both SR and SC and thus had a lower composite index score. This supports previous research that indicates depressed persons have better cognitive insight than patients with psychosis or bipolar disorder (Colis et al., 2006). Healthy adults had the lowest composite index score, due to their significantly lower SR scores, as well as an SC lower than the depressed group. Whilst previous research has identified that healthy adult groups produce the same factor structure as patients when completing the BCIS (Buchy, Brodeur & Lepage, 2012), the current study indicates that healthy adults do not score higher than FEP patients, unlike previously reported data (Kao et al., 2011), and are more in line with work indicating there is no significant difference between FEP and control groups (Engh et al., 2007). The FEP group in this study was significantly more depressed than the healthy group, which may explain the higher SR score, as the meta-analysis in chapter 6 indicated that better self-reflectiveness is associated with lower mood. Alternatively, it is suggested that FEP patients appear more self-reflective than healthy adults because they do indeed reflect more on their personal experiences and thoughts, as they are having unusual illness-related experiences (Bedford, 2010). However this is not to say that healthy adults have "worse" cognitive insight than FEP patients, perhaps instead they answer the BCIS differently to patient groups as they 1) do not have as much to reflect on, or 2) interpret questions differently. Further, SC scores did not differ between FEP and healthy adult groups. As discussed in chapter 7, high self-certainty does not necessarily represent a cognitive bias in healthy adults, but an assurance that one's beliefs are correct, as in this study's depressed group. Indeed, self-certainty is only problematic when twinned with low self-reflection, leading to cognitive rigidity (Riggs et al., 2012). Further, due to the potential variance in both self-reflection and self-certainty it is unlikely that a cut off score for cognitive insight will be identified that will enable us to accurately differentiate between patient and healthy groups (Martin et al., 2010). Healthy adults also scored lowest on the DEX self-report, however this is expected as they had less symptoms of dysexecutive syndrome compared to patient populations.

There was a near-significant difference between healthy older adults (>60 years old) and patients with ED on DEX independent rater scores, however this was not the case on self-reported DEX scores, and this did not lead to a significant difference in discrepancy scores. This indicates that perhaps adults with a diagnosis of dementia are more likely to be rated highly on the DEX, whereas self-ratings do not differ across groups. There was no difference, however, in the two groups' discrepancy scores, indicating that, overall perhaps there is no difference in awareness of dysexecutive symptoms between the two groups. This may also be explained by our use of patients with relatively good MMSE scores (mean 25.9); Zanetti et al. (1999) described a "tri-linear" account of insight, whereby patients scoring an MMSE greater than 24 consistently demonstrated better insight than those scoring below this, as described in Chapter 3.1.3.2. Research with patients scoring a wider range of MMSE scores would therefore be useful in the future.

There were a number of differences between the two clinical groups of interest regarding clinical scales of awareness. FEP patients sored significantly higher on BCIS self-reflectiveness and DEX self-rated scales, and SAI (questions 1-8). This result is in keeping with previous work by Gilleen, Greenwood & David (2009) indicating that patients with dementia score lower on the SAI than patients with schizophrenia. Post-hoc analyses indicated that FEP patients had higher rates of self-reported depression, which is known to be associated with higher self-reflection (chapter 6). Results therefore suggest that, on clinical measures of awareness, patients with dementia show worse awareness profiles regarding cognitive insight self-reflection, clinical presentation and symptoms and reflection about their executive function and daily functioning. This group difference may also be due to the FEP group scoring higher on measures of depression, as low mood is associated with better awareness in both clinical groups (Mintz et al., 2003; Aalten et al., 2005). Patients with ED did not show a significant difference compared to patients with FEP in their SC scores, as measured on the BCIS scale, indicating they are no more or less "overconfident" regarding their self-beliefs.

Now turning to memory metacognitive efficiency, results support the hypothesis that "patients experiencing their first episode of psychosis … will have lower metacognitive scores than healthy controls" as there were significant differences between healthy adults, depressed patients and FEP patients in both efficiency and confidence. Healthy adults and depressed patients scored comparably on both memory metacognitive efficiency and confidence in performance, whereas FEP patients had an overall worse mean efficiency score, despite no significant difference in task performance across groups, which is akin to results from previous work using FOK judgments (Bacon et al., 2001). However, the current study does not support results that measured metacognition using the gamma statistic (Souchay et al., 2006), which may be due to the use of less reliable statistical analysis (Masson & Rotello, 2009). Unlike clinical insight measures, depressed patients did not appear to have better self-awareness for these experimentally controlled tasks compared to healthy adults. This may be because these computerised objective ratings allow less time for rumination and prolonged consideration than self-report questionnaires, which are usually not time limited. Indeed, perhaps in the case of time-limited self-ratings, there is not time for a depressed bias towards "better" self- appraisal to manifest itself.

FEP patients also had significantly lower confidence ratings compared to healthy controls and depressed patients, and thus appeared to have less of a self-serving bias towards positive self-confidence (as indicated by mean confidence scores over 2). This was unexpected, as results from BCIS studies have often indicated that FEP patients are over-confident about their self-appraisal (Engh et al., 2007; Warman et al., 2007). Thus, it may be that this previously observed overconfidence in FEP is limited to illness-related self-awareness, suggesting that whilst this computerised task and BCIS both measure aspects of self-awareness, the two domains of metacognition are not related, further supporting conclusions made in chapter 8.

In contrast, novel results did not support the hypothesis that *"*patients experiencing … early-stage dementia ... will have lower metacognitive scores than healthy controls" as there was no significant difference in the metacognitive efficiency performance or confidence ratings between older adults and ED patients. It is perhaps possible that metacognitive efficiency, as measured by self-appraisal of task performance, is spared in the early stages of dementia, and memory metacognitive efficiency degrades at the same rate as observed in healthy older adults, despite the noted difference in memory and executive abilities between healthy and clinical groups. It is worth noting that the ED patients in our sample were relatively unimpaired in measures of general cognition (MMSE). As well, while some patients with MCI will never progress towards dementia, some apparently healthy older controls may be in fact experiencing sub-clinical pathological changes that precede MCI and AD. This situation of diagnostic MMSE classification would tend to blur differences between groups. An interesting further study would be to investigate the difference between patients with early and later stage dementia, to identify whether metacognitive processes are affected at later stages in the cognitive decline observed in dementia.

Finally, there were no significant differences observed in the memory metacognitive efficiency performance or confidence of FEP and ED patients. This therefore suggests that there is a greater degradation in memory metacognitive efficiency for FEP patients relative to their age compared to ED, who score comparably with their healthy age matched counterparts. Indeed, looking at the mean memory metacognitive efficiency scores, FEP patients appear to have a lower mean score than older adults; however they also have a larger standard deviation of scores. This therefore suggests that poor memory metacognitive function is more prominent and problematic for patients with FEP than those with ED. Previous research has indicated that awareness of executive and behavioural deficits is worse in dementia patients compared to those with schizophrenia (Gilleen et al., 2009). The current study therefore indicates that different domains of self-awareness, such as appraisal of one’s task performance versus appraisal of one’s behaviour or thoughts about illness experience, are affected to different degrees across diagnosis. Further investigations with larger sample sizes would be useful to confirm this hypothesis.

10.4.1 Conclusions

These findings indicate that patients with FEP indeed have different self-awareness profiles to those with ED, with varying deficiencies evident across awareness domains compared to healthy adults.

FEP patients showed no difference or indeed better awareness compared to healthy younger adults on self-report measures of self-awareness, which may be explained by higher depression scores in the FEP group. However FEPs showed significant impairment in metacognitive efficiency compared to their healthy counterparts, indicating that it may be the efficiency of their self-awareness that is more severely impaired in FEP than their ability to self-reflect. Interestingly, ED patients showed comparable self-reflection and metacognitive efficiency to their peers, indicating that in the early stages of dementia and cognitive impairment, awareness of cognitive and functional abilities may be comparable, despite a difference in actual abilities. When comparing the two patient groups, however, it was clear that there were domain specific differences in their awareness profiles. Similarly to Gilleen et al. (2009), FEP patients demonstrated a greater ability to self-reflect on their self-report questionnaires than ED patients. The current study has also demonstrated that there are no differences in metacognitive efficiency between groups; as there is a known age related decline in metacognitive efficiency these results indicate that there is a greater impairment in the FEP group relative to their age than in ED patients.

CHAPTER 11

11. VOXEL BASED MORPHOMETRY STUDY OF THE ASSOCIATION BETWEEN METACOGNITIVE EFFICIENCY AND BRAIN STRUCTURE IN PATIENTS WITH EARLY STAGE DEMENTIA.

METHODS AND RESULTS FOR IMAGING ANALYSIS

The aim of the work presented in this chapter was to identify the structural neural correlates of metacognitive efficiency in patients with early stage dementia (ED). Due to the low number of patients successfully completing the perceptual metacognitive task, only memory metacognitive efficiency was studied in this analysis. A second aim was to identify neural correlates of BCIS scores in the same group of patients, and identify if these are similar to those associated with metacognitive efficiency. This chapter details the methods utilised to analyse the structural MRI data, and describes the findings.

11.1 IMAGING METHODOLOGY

This section will detail the Magnetic Resonance Imaging (MRI) acquisition, pre-processing and statistical analysis methods that were used when analysing brain MRI data. Whole group means and demographics are reported in chapter 9. This analysis includes 15 patients in the ED group who had an MRI scan within 5 months of completing the metacognitive test. Of the 15 patients who had an MRI scan, 2 had no meta d'/d' score (as they were unable to complete the task) and 2 had a d' score <0.25, and were thus removed from the metacognitive efficiency analysis. Demographics for this subset of 15 patients are reported in section 11.2.1

Voxel-based morphometry (VBM) is a neuroimaging analysis technique performed on structural MR images to identify the effects of a given variable of interest on brain structure (Ashburner & Friston, 2000); enabling investigation of significant differences in brain anatomy, using the statistical approach of statistical parametric mapping. VBM can be used to analyse differences in brain structure between groups or identify a relationship in one group between brain structure and a given variable, such as age or score on a particular task. When VBM is conducted to study the relationship between brain structure and a given variable, the null hypothesis states that there is no correlation between tissue volume and the variable in question. Specifically for the present study, the null hypothesis is that there will be no correlation between brain tissue volume and metacognitive efficiency in ED patients.

As is common in the VBM literature, in this thesis it will be assumed that region of interest (ROI) size is driving the differences in VBM signal. However, it is noted that there may be subtler anatomical shape variations creating the VBM signal differences (Ashburner & Friston, 2001; Whitwell, 2009). In other words, although we assume that it is the volume of a particular structure that is associated with a variable, VBM cannot discount the possibility that differences in the shape of the ROI are contributing to the difference in VBM signals across patients (Bookstein, 2001).

MR Images were collected as part of the “Plasma Based Biomarkers for Alzheimer’s Disease” study at the Centre for Neuroimaging Sciences, Institute of Psychiatry (ethics approval number 06/Q0706/50), using a General Electric SIGNA HDx 1.5T MR scanner. The neuroimaging protocol was designed for compatibility with the Alzheimer's Disease Neuroimaging Initiative (ADNI) magnetic resonance (MR) protocol and has been presented in detail previously (Jack et al., 2008; Simmons et al., 2009, 2011). Briefly, the protocol was implemented in the local high-resolution sagittal 3D T1-weighted MP-RAGE ‘adni14m4’ pulse sequence (slice thickness 1.2mm, slice gap 1.2mm, matrix size 192x192 with 180 spatial slices, voxel size 1.2 x 1.2 x 1.2mm, flip angle 8 degrees). Repetition Time was 8.6 seconds, and Echo Time was 3.8 seconds.

11.1.1 IMAGE PRE-PROCESSING

A fundamental problem with analysing brain structure across or within groups is that there are substantial individual differences in large-scale brain anatomy, in terms of global head size, as well as the size and shape of particular brain structures across a participant sample, which are due to natural anatomical variability rather than the effect of interest (Ashburner & Friston, 2001). For instance, people with larger heads will usually have uniformly larger brain volumes, which can confound the analysis if not taken into consideration, as significant between or within group differences may actually be the spurious result of these factors. VBM analysis helps overcome this problem by using a number of processes to register the MR images of interest in the same “normalised” anatomical space or template. Individual scans are spatially matched (registered) to the template, resulting in a given location in this template corresponding approximately to the same anatomical location in each one of the individual normalised scans. This process allows brain anatomy to be more quantitatively compared irrespective of global variations in brain anatomy. This process is known as spatial normalisation. Fig 11.1-2 shows an example of the gray matter template employed in this study.

The process of VBM begins with “Segmentation”, which essentially identifies and separates the scan into one of four tissue types; gray matter, white matter, cerebrospinal fluid (CSF) and miscellaneous residual category of other tissues (such as skull and skin of the scalp). The default segmentation process (in this study performed using the “new segment” toolbox in SPM8) warps the individual brains to a template anatomical space, so that they are aligned in terms of macroscopic characteristics, and therefore global differences in head size and large-scale morphological differences are corrected for, allowing accurate comparisons of structures to be made independently of large-scale anatomical variability.

The MR images are constituted by volumetric image elements, or voxels, which are the basic elements of brain anatomy measurement. In an analogy with the basic constituents of a 2D image or pixels, voxels can be understood as “3D pixels”. In the present study, the image acquisition sequence produced voxels of size $1.2mm^3$, resulting in approximately 868000 voxels in each subject’s brain (assuming an average brain size of 1500 cc). The segmentation algorithms assume every voxel in the scan is constituted by different proportions of the four tissue types; gray matter, white matter, CSF and other tissues (such as skull and skin of the scalp; Ashburner & Friston, 2005) and creates separate images for each type of tissue (see figure 11.1-1 for the first three). In the present study only gray matter images for each subject were used in the second stage analysis, as the primary hypothesis of the locus of association between metacognitive abilities and brain structure concerned gray matter loss. Further, our patient population was constituted of patients with early stage dementia, and therefore with neurodegeneration primarily affecting gray matter. The segmented images for all tissue types were also added up to estimate total intracranial volume (TIV), which was then used as a covariate in the group analysis stage to account for residual differences in head size.

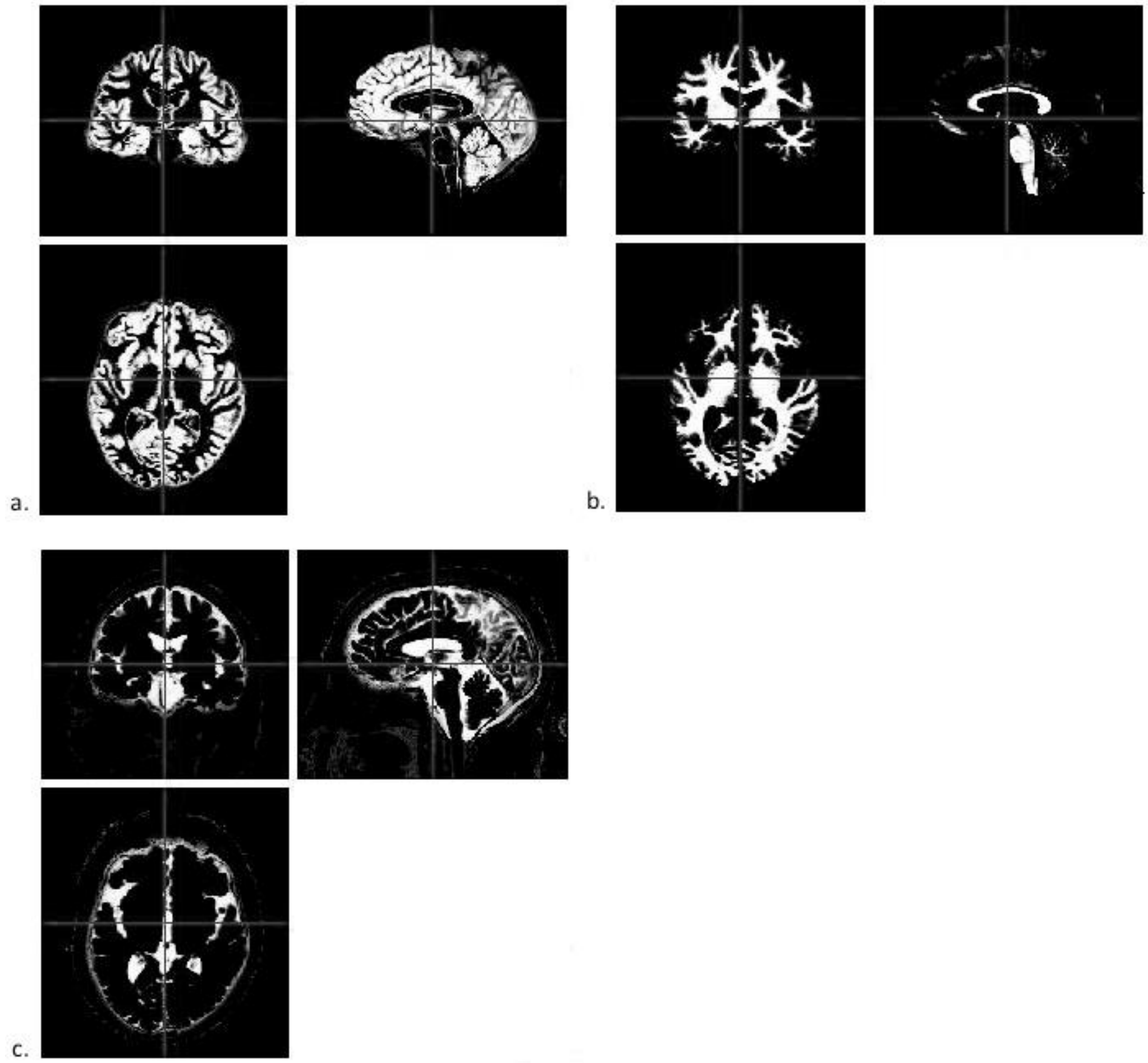


Figure 11.1-1 Illustrates one patients' MR image from this study (coronal, sagittal and axial views) after the segmentation process, a. gray matter, b. white matter, c. CSF.

After the process of Segmentation, the spatially normalised template is created by averaging all individual scans through DARTEL (diffeomorphic anatomic registration via an exponentiated lie algebra algorithm). This procedure increases the accuracy of inter-subject alignment (Ashburner, 2007). DARTEL is achieved by modelling the shape of each brain using three parameters for each voxel (resulting in over 2.5 million parameters per subject). DARTEL simultaneously aligns gray and white matter among all the data included in the analysis. This is achieved by generating average template data (see figure 11.1-2), to which the full data set are iteratively aligned.

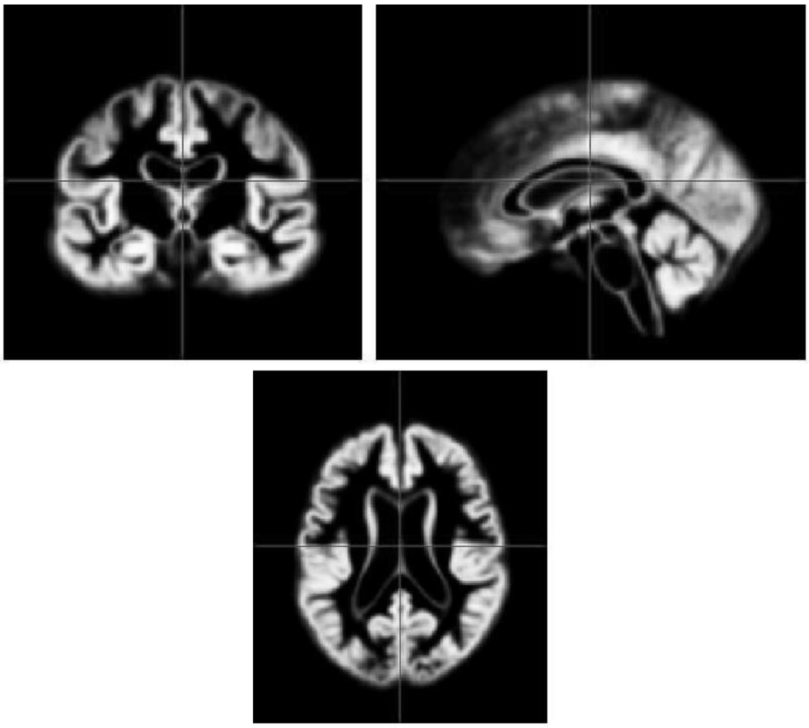


Figure 11.1-2 Illustrates DARTEL gray matter template for this study, which will be normalised to fit the MNI template in the final stage of pre-processing (coronal, sagittal and axial views).

In order to accurately compare data across patients, all images need to be in the same 3D space, which is achieved by the process of normalisation. Here the DARTEL template is “normalised” (i.e. shifted and warped) to fit the Montreal Neurological Institute (MNI; Evans, Janke, Collins, & Baillet, 2012) template and then the deformations are used to normalise the segmented images to the MNI space. Once this has been completed the images are smoothed (usually 8mm FWHM [full-width at half-maximum] Gaussian kernel) creating spatially normalised and Jacobian scaled (taking into account how each data set has been adjusted individually to fit the template) gray matter images in MNI space (see figure 11.1-3).

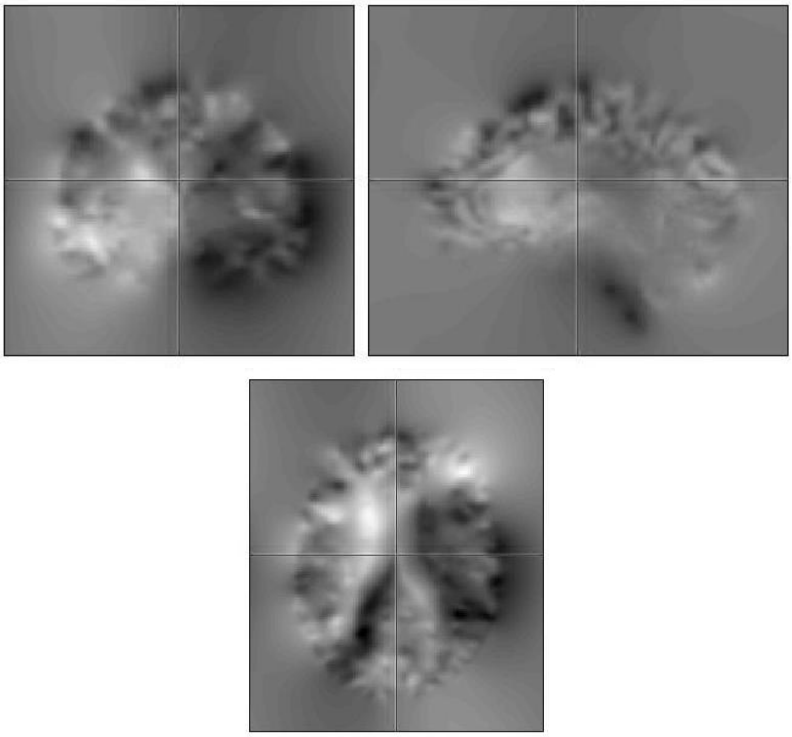


Figure 11.1-3 Illustrates NMI normalisation smoothed images for one patient from this study (coronal, sagittal and axial views).

In the current study VBM was used to identify any differences in brain structure (e.g. volume of a specific area) and if this is related to metacognitive efficiency. This procedure was completed by closely following the methodology described in John Ashburner's 2010 VBM tutorial for SPM-8. (http://www.fil.ion.ucl.ac.uk/~john/misc/VBMclass10.pdf; see appendix 11.1.1 for code used for batch processing).

11.1.2 Statistical Analysis

Statistical analysis was carried out using SPM version 8 (http://www.fil.ion.ucl.ac.uk/spm/) on MatLab. Before analysis could be carried out, total intracranial volume (TIV) was estimated to use as a covariate. This was carried out using code obtained from the SPM mailing list (spm@jiscmail.ac.uk) archives (https://www.jiscmail.ac.uk/cgi-bin/webadmin?A0=spm) (see appendix 11.1.2 for script). This script was run for gray matter, white matter and CSF volume, with these three values being combined to calculate the TIV. Multiple regression analysis was carried out to investigate the relationship between memory meta d'/d' scores and brain structure (gray and white matter volume), co-varying for TIV and age (see appendix 11.1.3 for script). We restricted our reported findings to gray matter regions, as findings in white matter where likely to be artefacts.

The null hypothesis was tested at two anatomical levels: a region of interest (ROI) approach focusing on replication of the findings by Fleming et al. (2010) in healthy adults in our ED sample, followed by a whole-brain exploratory analysis. For the ROI analysis, the automatic anatomical labelling (AAL) atlas (http://qnl.bu.edu/obart/explore/AAL/) was employed to obtain a Brodmann area 10 (BA10; anterior prefrontal cortex) mask. In this analysis the null hypothesis was tested using strict multiple comparisons correction based on random field theory adjusted with an appropriate correction for the small search volume. This analysis was followed by an exploratory whole brain analysis, conducted at an uncorrected threshold of $p<0.001$. The locations of significant effects were approximated using xjview toolbox (http://www.alivelearn.net/xjview8/) on SPM-8, using the AAL atlas (http://qnl.bu.edu/obart/explore/AAL/) and entering peak voxel coordinates identified in whole brain analysis.

11.2 Results

11.2.1 Demographics

BCIS

A total of 15 patients with early-stage dementia (ED) were included in the BCIS part of this study, mean age 78.5 (±8.64), of whom 7 were women (46%). There was no significant difference in age by gender in this sample. 13 people (86.6%) in the sample identified as White (British/Irish/European/American); 1 person identified as Asian and 1 identified as Black African. 10 of the patients in the sample had a diagnosis of Mild Cognitive Impairment (MCI) and 5 had a diagnosis of Mild Alzheimer's Disease (AD). The mean MMSE score of this group was 26.5 (±2.54).

Metacognition

A total of 11 patients with early-stage dementia (ED) were included in the metacognition portion of this study, mean age 77.6 years (±7.60), of whom 4 were women (36%). There was no significant difference in age by gender in this sample. 9 people (81%) in the sample identified as White (British/Irish/European/American); 1 person identified as Asian and 1 identified as Black African. 7 of the patients in the sample had a diagnosis of Mild Cognitive Impairment (MCI) and 4 had a diagnosis of Mild Alzheimer's Disease (AD). The mean MMSE score of this group was 26.5 (±2.70).

11.2.2 Metacognition

Coordinates	**Cluster size/no of voxels**	**Anatomical Label**	**Brodmann area**	**t-value**	**Direction of association**
3, -7, 40	96	Right dorsal anterior cingulate	32	6.31^	+
60, -27, 48	34	Right post-central gyrus	1,2,3	6.26^	+
-33, 87, -33	45	Left posterior cerebellum	n/a	5.46^	+
-4, -13, -30	58	Left brainstem	n/a	5.40^	-
33, -82, 12	17	Right middle occipital gyrus	19	4.04^	-

Table 11.2-1 Shows significant associations between memory metacognitive efficiency and various brain regions, where "+" denotes a positive association and "-" denotes a negative association, and ^p<.001 uncorrected.

There was no significant association between BA10 gray matter volume and memory metacognitive efficiency in ED patients (corrected at p<0.05 family wise error [FWE] based on random field theory with small search area correction).

An additional exploratory whole brain analysis was then conducted, as is frequent in neuroimaging, at the relatively lenient threshold of at the p<.001 level, resulting in a number of significant positive correlations (see figure 11.2-1 for 3D rendered image, figure 11.2-2 for axial slice images). A significant correlation between metacognitive efficiency and gray matter in the right dorsal anterior cingulate (figure 11.2-3, peak voxel coordinates: [3, -7, 40]; tmax = 6.31; p< 0.001, uncorrected); the right post central gyrus (figure 11.2-4, peak voxel coordinates: [60, -27, 48]; tmax = 6.26; p< 0.001, uncorrected) and the left posterior cerebellum (peak voxel coordinates: [-33, -87, 40]; tmax= 5.46; p< 0.001, uncorrected)

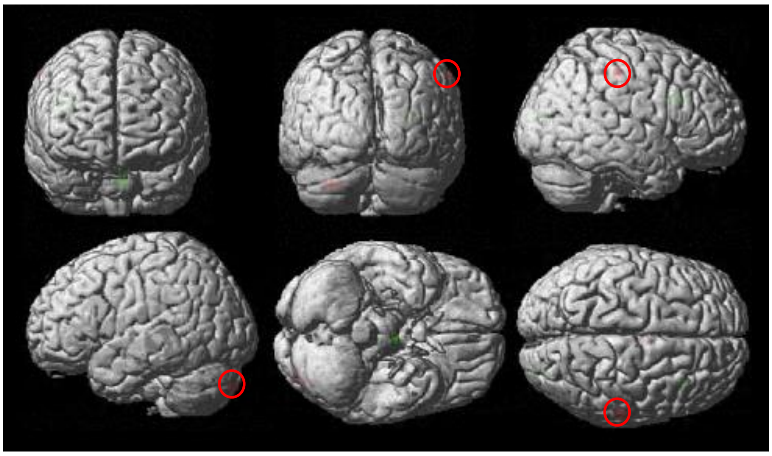


Figure 11.2-1 3D rendered image, showing areas in which gray matter volume correlates positively with memory meta d'/*d'*. The significant clusters indicated with red blobs (and red circles where necessary).

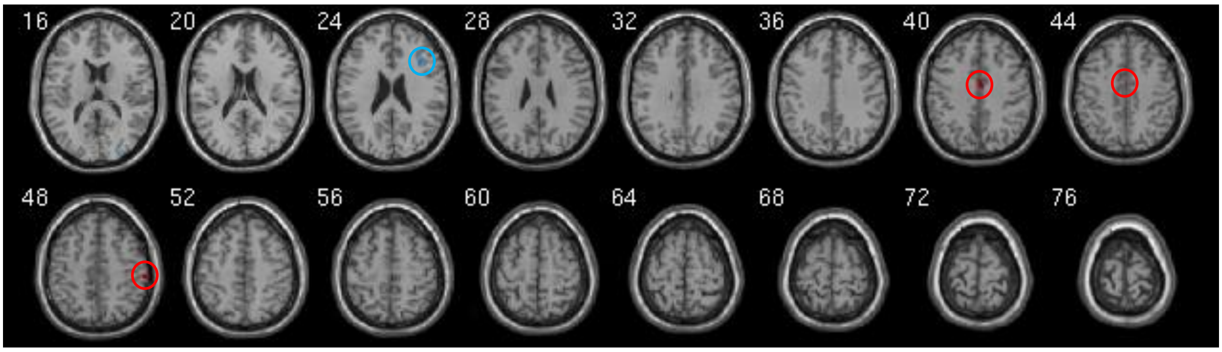


Figure 11.2-2 Axial slices (4mm spacing) showing areas in which gray matter volume correlates positively with memory meta d'/*d'*. The significant positive clusters indicated with red blobs and red circles (slices, 32, 40, 44) and negative clusters indicated with blue blobs and blue circles (slice 24)

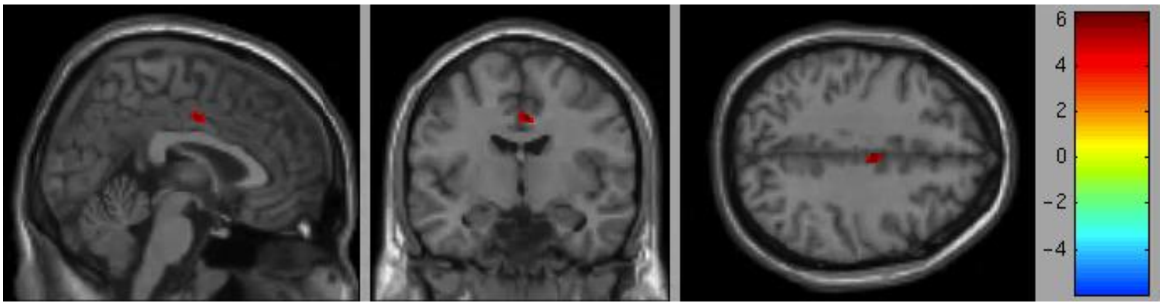


Figure 11.2-3 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with memory meta d'/*d*' (red blobs). The significant cluster was found in the right dorsal anterior cingulate.

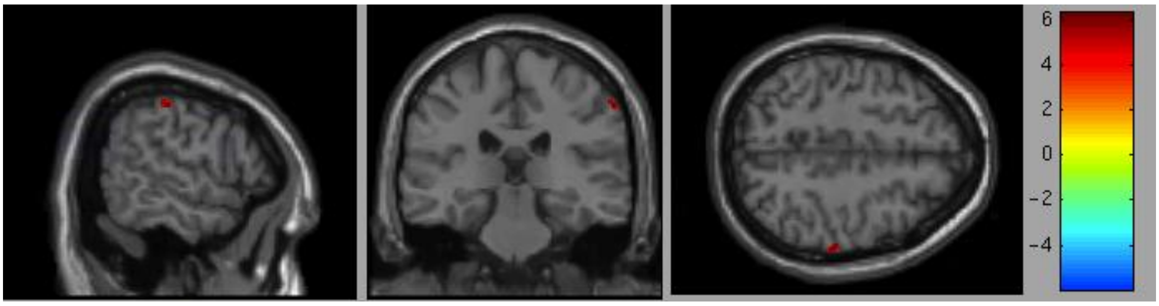


Figure 11.2-4 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with memory meta d'/*d*' (red blobs). The significant cluster was found in the right post central gyrus.

There were also significant negative correlations between meta d'/d' and volume of the left brainstem (peak voxel coordinates: [-4, -13, -30]; tmax= 5.40; p<.001, uncorrected) and the middle occipital gyrus (peak voxel coordinates: [33, -82, 12]; tmax= 5.04; p<.001, uncorrected). However, none of the metacognitive efficiency results survived correction for multiple comparisons across the brain volume.

11.2.3 Cognitive Insight

11.2.3.1 Self-reflection

Coordinates	Cluster size/no of voxels	Anatomical Label	Brodmann area	t-value	Direction of association
60, 20,-11	21	Right inferior frontal gyrus	45	4.84^	+
-22, 32, -15	44	Left middle frontal gyrus	46	4.82^	+
-40, -88,-14	18	Left inferior occipital gyrus	19	4.13^	+
-21, -79, 12	55	Left cuneus	17	6.03^	-
15, -43, -3	104	Right parahippocampal gyrus	34	4.70^	-
15, -72, 12	31	Right cuneus	17	4.19^	-

Table 11.2-2 Shows significant associations between SR and various brain regions, where "+" denotes a positive association and "-" denotes a negative association, and ^p<.001 uncorrected.

An exploratory whole brain analysis was conducted at the p<.001 level, which produced a number of significant correlations (see figure 11.2-5 for 3D rendered image, figure 11.2-6 for axial slice images). A significant positive correlation between SR scores and volume of the frontal lobes; the right inferior frontal gyrus (figure 11.2-7, peak voxel coordinates: [60, 20, -11]; tmax = 4.84; p<.001, uncorrected), the left middle frontal gyrus (figure 11.2-8, peak voxel coordinates: [-22, 23, -15], tmax = 4.82; p<.001, uncorrected); as well as the left inferior occipital gyrus (peak voxel coordinates [-40 -88 -14]; tmax = 4.13; p<.001, uncorrected)

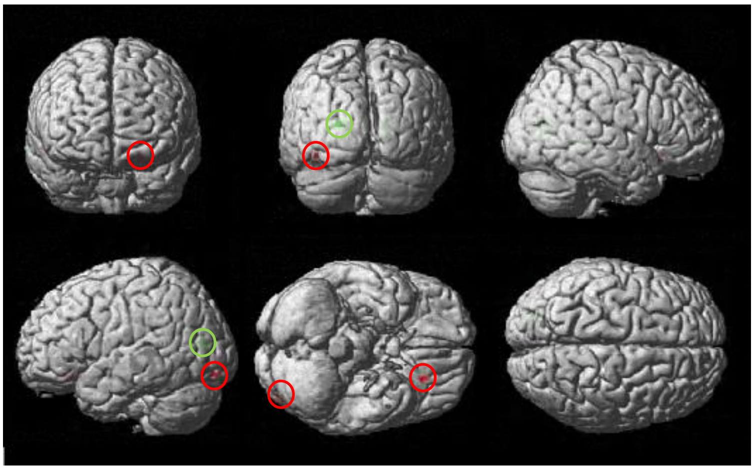


Figure 11.2-5 3D rendered image, showing areas in which gray matter volume correlates positively with SR. The significant clusters indicated with red (highest correlation) and green (smaller correlation) blobs.

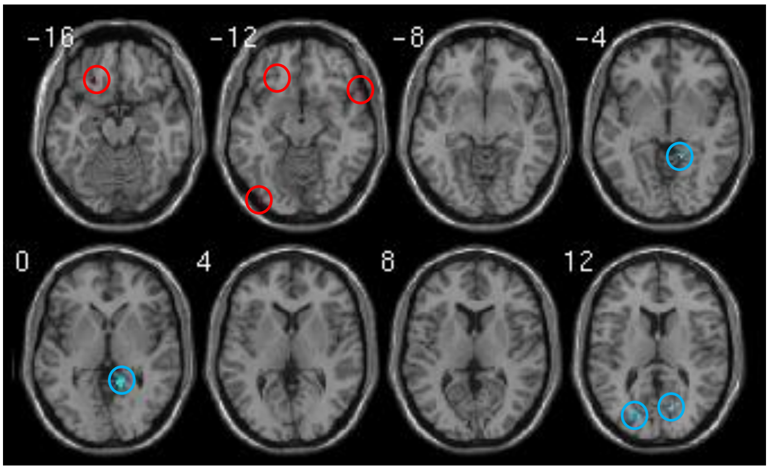


Figure 11.2-6 Axial slices (4mm spacing) showing areas in which gray matter volume correlates with SR. The significant positive clusters indicated with red (slices -16, -12), significant negative clusters indicated in blue (slices 0, 12).

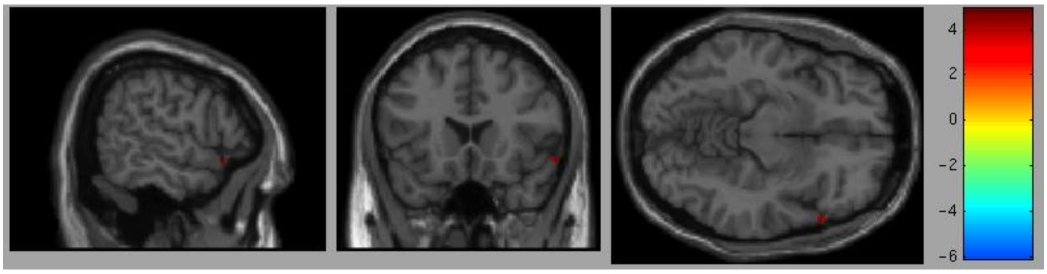


Figure 11.2-7 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with SR (red blobs). The significant cluster was found in the right inferior frontal gyrus.

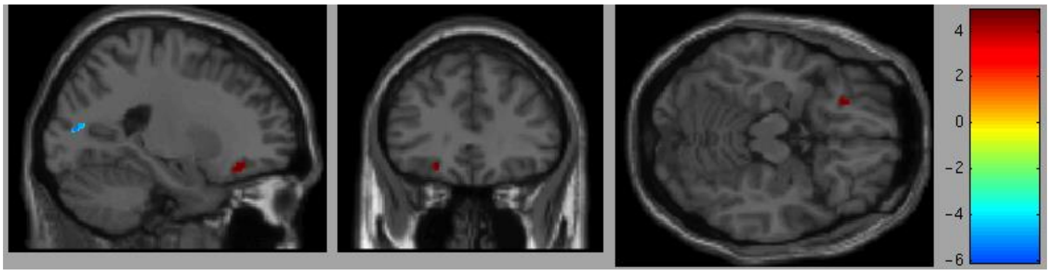


Figure 11.2-8 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with SR (red blobs). The significant cluster was found in the left middle frontal gyrus.

There were also significant negative correlations between BCIS SR and volume of the right parahippocampal gyrus (peak voxel coordinates: [15 -43 -3], tmax = 4.70; p<.001, uncorrected), the right cuneus (peak voxel coordinates: [15, -72, 12]; tmax = 4.19; p<.001, uncorrected) and left cuneus (peak voxel coordinates: [-21, -79, 12]; tmax=. 6.03; p<.001, uncorrected).

However, none of the self-reflection results survived correction for multiple comparisons across the brain volume.

11.2.3.2 Self-certainty

Measure & direction of association	Coordinates	Cluster size/no of voxels	Anatomical Label	Brodmann area	t-value
+	-12, 8, -15	294	Left subcallosal gyrus	25	11.53*
+	-48, -45, -5	41	Left middle temporal gyrus	46	5.24^
+	46, 8, 7	128	Right precentral gyrus	4	5.08^
+	16, 24, 37	11	Right dorsal anterior cingulate	32	4.54^
+	-12, 27, 25	29	Left anterior cingulate	32	4.38^
-	33, -96, -6	121	Right left middle occipital gyrus	19	5.12^
-	46, 60, 7	53	Right middle frontal gyrus	10	4.85^

Table 11.2-3 Shows significant associations between SC and brain regions, where "+" denotes a positive association and "-" denotes a negative association. *p<.01 corrected for FWE, ^p<.001 uncorrected.

An exploratory whole brain analysis was conducted at the p<.001 level, which produced a number of significant correlations (see figure 11.2-9 for 3D rendered image, figure 11.2-10 for axial slice images). A significant positive correlation between BCIS SC scores and volume of the frontal lobes; the left subcallosal gyrus (figure 11.2-11, peak voxel coordinates: [-12, 8, -15]; tmax = 11.53; p<.001, uncorrected; left middle temporal gyrus (peak voxel coordinates: [-48, -45, -5]; tmax = 5.24; p<.001); right precentral gyrus (figure 11.2-12, peak voxel coordinates [46, 7, 8]; tmax = 3.64; p<.001); left anterior cingulate(figure

11.2-13, peak voxel coordinates: [-12, 27, 25]; tmax = 4.38; p<.001) and the right dorsal anterior cingulate (figure 11.14-21, peak voxel coordinates: [16, 24, 37]; tmax = 4.54; p<.001).

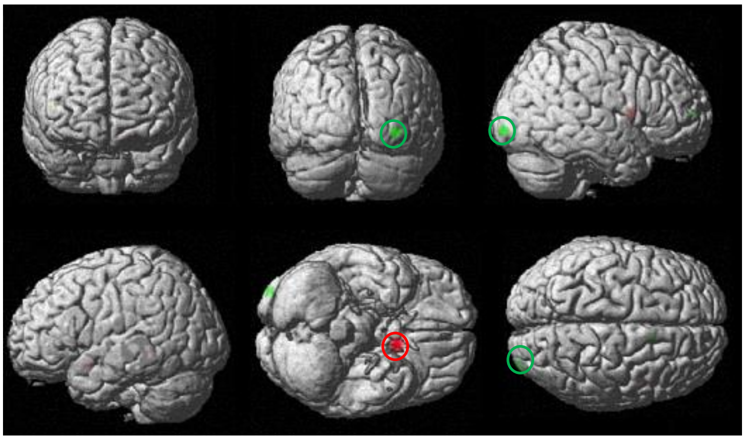


Figure 11.2-9 3D rendered image, showing areas in which gray matter volume correlates with BCIS SC. The significant clusters indicated with red and green blobs (positive).

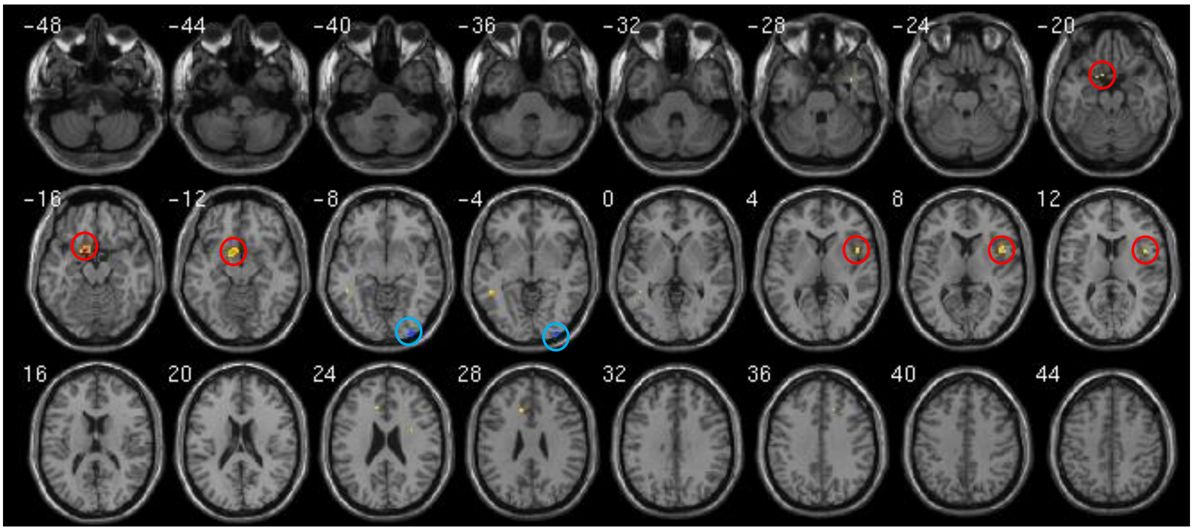


Figure 11.2-10 Axial slices (4mm spacing) showing areas in which gray matter volume correlates with BCIS SC The significant positive clusters indicated with red and yellow (slices –20, -16, -12, -8, -4, 4, 8, 12), significant negative clusters indicated in blue (slices -8, -4).

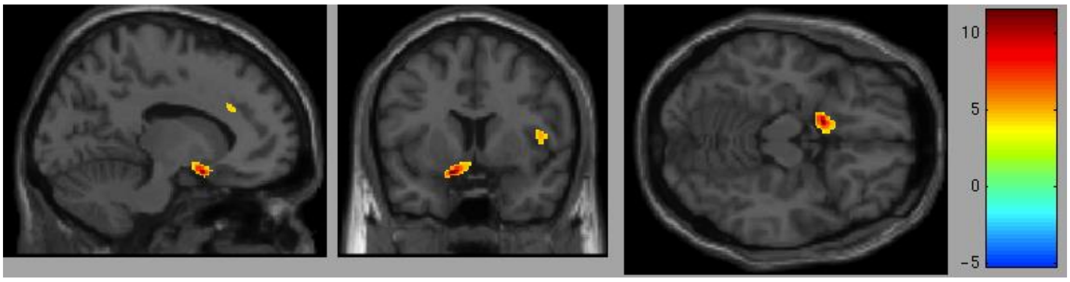


Figure 11.2-11 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with BCIS SC (red and yellow blobs) . The significant cluster was found in the left subcallosal gyrus,

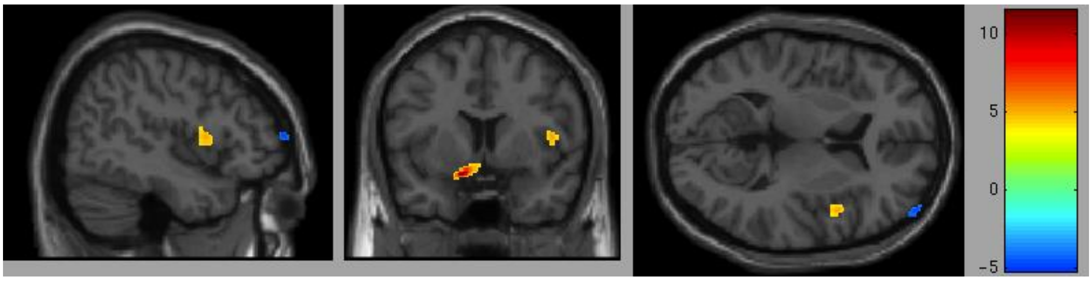


Figure 11.2-12 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with BCIS SC (yellow blobs) The significant cluster was found in the right precentral gyrus.

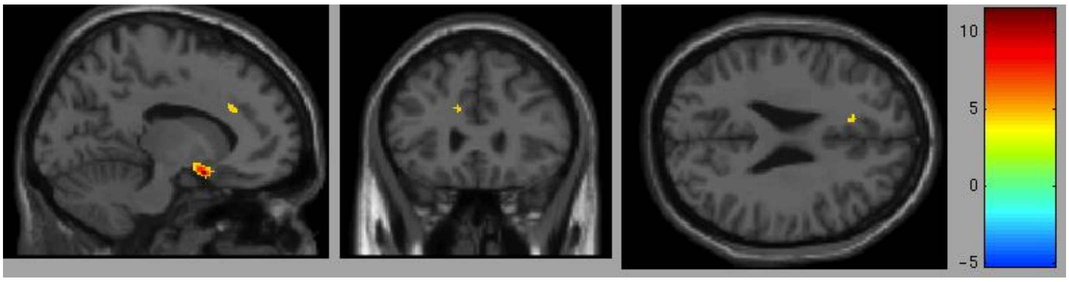


Figure 11.2-13 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with BCIS SC (yellow blobs). The significant cluster was found in the left anterior cingulate.

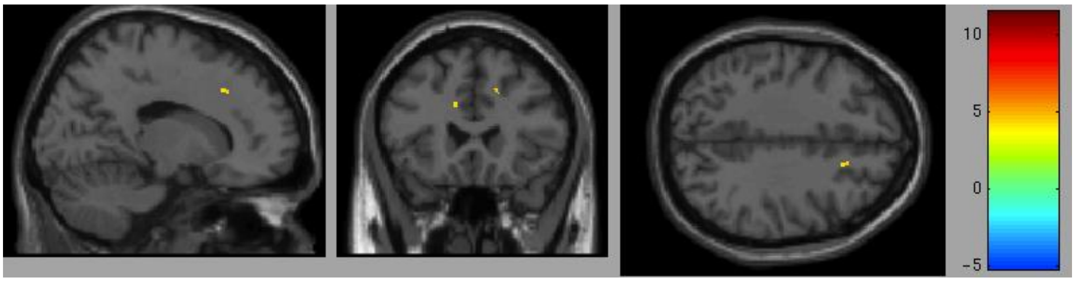


Figure 11.2-14 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with BCIS SC (yellow blobs). The significant cluster was found in the right dorsal anterior cingulate.

There were also significant negative correlations between BCIS SC and gray matter; right middle occipital gyrus (peak voxel coordinates: [33, -96, -6], tmax = 6.03; p<.001), right middle frontal gyrus/BA10 (see figure 11.2-15 [46, 60,7] tmax = 4.85; p<.001).

The only result that survived correction for multiple comparisons across the brain volume was the positive association between SC and the left subcallosal gyrus (p<.01).

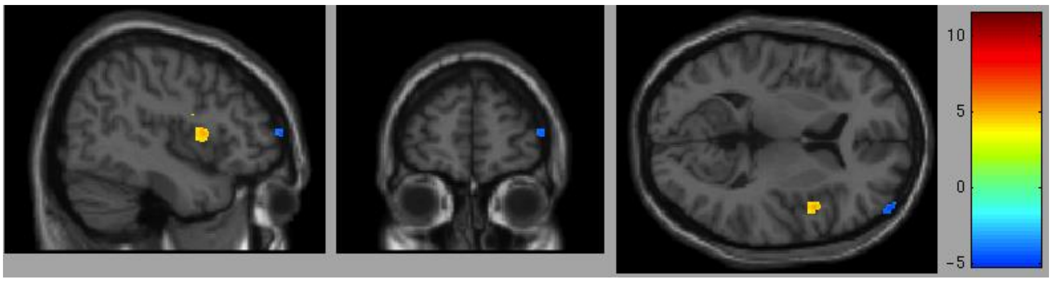


Figure 11.2-15 Statistical (*T*) maps shown on a standard overlay (coronal, sagittal and axial views) showing areas in which gray matter volume correlates positively with BCIS SC (blue blobs). The significant cluster was found in the right middle frontal gyrus (BA10 area).

11.3 Discussion

The aim of this chapter was to test the null hypothesis that there will be no correlation between brain tissue volume and metacognitive efficiency in ED patients, and conduct an exploratory analysis to investigate the neural basis of cognitive insight in a group of patients with early stage dementia.

There was no significant correlation between meta d'/d' and the BA10 area of the frontal lobe, which was identified as being related to perceptual metacognitive efficiency by Fleming et al. (2010), and thus the hypothesis "There will be a significant relationship between areas of the frontal lobe, such as the BA10" is not supported. This may be due to the low number of patients included in this analysis, compared to the 32 included in the original study, causing this study to have less power and thus produce null results. Another reason for this lack of association may be that the current study analysed the relationship with memory metacognitive efficiency and previous studies have analysed perceptual metacognitive efficiency. Indeed, a study by McCurdy et al., (2013) found there to be little overlap in the neural correlates of memory and perceptual metacognition in healthy young adults, where the only similar neural correlate between both domains of metacognition was part of the precuneus, which may explain the lack of association in our study with BA10. Though this thesis indicates that there is a significant association between the two domains of metacognitive efficiency in healthy adults (reported in chapter 7), no such association was identified in the early stage dementia group. This is most likely due to the low number of patients who successfully completed the perceptual metacognitive task, however it may be that perceptual metacognitive efficiency is associated with BA10 volume, but memory metacognitive efficiency is not. As well, this study included patients with neurodegeneration, resulting in a more heterogeneous population than the sample of healthy young adults presented in Fleming et al (2010). A heterogeneous sample usually results in increased variability of the measurement and therefore less statistical power, all else being equal.

The exploratory analysis, however, identified areas of positive association between metacognitive efficiency and gray matter volume, predominantly in frontal regions sub-serving executive processes, known to be associated with atrophy in MCI patients (Driscoll et al., 2009). Analysis found there was a significant positive association between metacognitive efficiency and gray matter in the dorsal anterior cingulate cortex, which has previously been associated with awareness of cognitive deficits and responses to and detection of errors in healthy older adults and patients with dementia (Ries et al., 2012; Sultzer et al., 2013).

Further associations were found between metacognitive efficiency and right post central gyrus, which is part of the parietal lobe. Literature surrounding dementia patients has indicated that the right parietal lobe is associated with insight into memory difficulties (Cosentino & Stern, 2005).

Results also indicated a positive correlation with the right cerebellum and significant negative correlation with the left brain stem. These areas are likely artefacts as neither is related to awareness in dementia or MCI related volumetric changes (Liu et al., 2010; see section 11.3.1 for further details of limitations)

However, results reported in chapter 10 demonstrated that there was no difference in memory metacognitive efficiency between healthy older adults and ED. It was therefore suggested that, in the ED group, there was no significant difference in the deterioration of metacognitive efficiency or self-awareness over and above that observed in healthy ageing (discussed in chapter 7), and that dementia-related deterioration associated with gray matter atrophy occurs when and if early dementia progresses to Alzheimer’s dementia. One possible explanation for the lack of a clear-cut clinical-pathological correlation in the ED group is that the relationship between variation in the volume of frontal structures and metacognitive efficiency is associated with neural correlates of normal ageing and hence would not differentiate ED patients from elderly controls. Further research into structural correlates of metacognitive efficiency in both healthy ageing and later stages of dementia will be required to clarify if this is the case.

There was a significant relationship between both BCIS sub-scale scores, SC and SR, and a number of brain regions. Of particular interest was the finding that SC was negatively associated with the right middle frontal gyrus (an area within the BA10 frontal region) while SR was positively associated with right inferior and left middle frontal gyrus (both adjacent to the BA10 area). These ROIs are all within the aPFC, which is associated with perceptual and visual metacognitive ability (Baird et al., 2013; Fleming et al., 2012; Fleming et al., 2010; Rounis et al., 2010), as well as attributive metacognition (Saxe, Schulz, & Jiang, 2006) in healthy adults. Further, functional imaging has demonstrated that activation of the PFC is associated with discrepancy scores on clinical memory questionnaire in MCI and AD patients (Vogel et al., 2005) and the bilateral medial PFC is associated with insight into illness and cognitive deficits in patients with dementia (Ries et al., 2012; Sultzer et al., 2013). Of particular interest is the direction of these associations. One may expect self-reflection (where a high score is deemed "better" on the BCIS) to be associated with better metacognitive efficiency, and self-certainty (where a high score is deemed "worse", as it denotes overconfidence) to be associated with less efficient metacognitive judgements. These imaging data demonstrate a positive association between self-reflection and the aPFC volume and a negative association with self-certainty and volume of this region, in agreement with these predictions. Behavioural results from this set of ED patients (reported in chapter 9) indicated that there was a significant positive association between perceptual metacognitive efficiency and BCIS SR, and a non-significant negative association with the BCIS SC. While there were no significant correlations between memory metacognitive efficiency and either SC or SR, the direction of the associations did indicate that there was a positive correlation with SR and a negative correlation with SC. In both measures of metacognitive efficiency their association with cognitive insight, whether significant or not, was consistent with the direction of associations with the aPFC respectively. The lack of significance in both behavioural and neuroimaging data indicates that perhaps the neuroimaging data has more statistical power than behavioural data due to less environmental confounds (such as fatigue), and less measurement variability (brain structure does not change markedly within hours or days, whilst performance can). It may be the case that larger sample sizes in a behavioural study, as suggested in chapter 9, would provide enough data and power to draw more robust conclusions, and perhaps results that would survive correction for multiple comparisons.

Further, SC scores were positively associated with the left subcallosal gyrus volume, a finding that survived correction for multiple comparisons, as well as the adjacent left anterior cingulate, and the right dorsal anterior cingulate volumes. There was also a significant association between SC scores and the right dorsal anterior cingulate, indicating that both hemispheres may be involved in self-certainty ratings. This left anterior cingulate finding is of interest because it and surrounding areas were also associated with memory metacognitive efficiency in studies of healthy participants. It is proposed that the ACC is involved in detection and response to errors (Ries et al., 2012), as well as strategic metacognition in healthy adults (Braver, Barch, Gray, Molfese, & Snyder, 2001; Wager et al., 2005) and was also found in this study to be significantly associated with memory metacognitive efficiency.

A number of unexpected associations were also found during this exploratory analysis. A positive association was found between SR and the left inferior occipital gyrus, as well as a negative association with SC and the right middle occipital gyrus, an area which is usually associated with reading and word recognition as part of a semantic processing network (Vandenberghe, Price, Wise, Josephs, & Frackowiak, 1996), but has not yet been associated with any measure of awareness in dementia. There was also a negative association identified between SR and the right parahippocampal gyrus, which is one of the main areas noted to atrophy in patients with MCI and AD dementia (Galton et al., 2001; Liu et al., 2010). This result was unexpected; behavioural studies have indicated that self-reflection is not associated (positively or negatively) with memory in schizophrenia patients (Nair et al., 2014), and a lack of association with memory function was also clear in this patient group (reported in chapter 9). SR scores were also found to be negatively associated with the left and right cuneus volumes. This region is not associated with early significant loss of volume or cortical thickness in MCI or AD (Liu et al., 2010) nor has it been associated with any measure of awareness in dementia. SC score was also positively associated with the left middle temporal gyrus, which is associated with volume loss in MCI and AD (Liu et al., 2010) but not awareness of cognitive decline. Finally, SC scores were associated with the right pre-central gyrus, an area of the primary cortex that is not known to be associated with awareness in dementia, but has been observed to atrophy in AD patients (Liu et al., 2010; see section 11.3.1 for further details of limitations). These unexpected results may be due to the increased threshold utilized in this this study to include uncorrected data, as there was only one significant result that survived more stringent thresholds (sub-callosal volume and SC). It can therefore not be excluded that these might be false positive results.

11.3.1 Limitations

All but one set of MRI results did not survive correction for multiple comparisons across the brain volume. This is to be expected due to the low number of participants included in the study (Whitwell, 2009). Studies with larger sample sizes should be conducted to confirm the results presented in this chapter. In particular structural MRI work looking at cognitive insight in early stage dementia would be worthwhile. Our focus on patients in the early stages of cognitive impairment led to the inclusion of MCI subjects. Some of these MCI patients may not progress on to develop dementia and do not suffer from a neurodegenerative condition. This could have resulted in a heterogeneous patient sample that could have reduced statistical power. Further, recent work by Spalletta et al. (2014) has indicated that there are structural differences in the early stages of dementia between patients diagnosed with MCI who go on to develop AD and those who do not. As our sample contained MCI and early-stage AD patients these structural differences in grey matter in areas of the CMS may also have confounded our results. Longitudinal studies as well as cross sectional studies with a larger range of diagnoses would be useful to further investigate this issue.

Though some results reported in this chapter are puzzling, this was a pilot exploratory analysis and thus it may not be possible to explain all the results reported in relation to previous literature. Larger experiments into cognitive insight in early stage dementia, with more power and a reduced significance threshold, are required to confirm how these unexpected associations should be interpreted.

Templates used in VBM analysis, such as the MNI, are created using “normal” healthy brains (Evans et al., 2012). As this sample used brains of patients with ED, there are some volumetric structural differences (Liu et al., 2010). It has been suggested that customised templates can be used to help minimize the chance of these errors occurring, however this would be of little use when we are interested in replicating results found in healthy populations. Further, due to the small sample size it was not possible to create a specialised template for this study.

11.3.2 Conclusions

Results partially supported this chapter’s hypothesis, as significant positive associations were identified between memory metacognitive efficiency and the dACC region of the cortical midline structures (CMS). Further to previous research, evidence suggests that specific regions of the CMS are associated with metacognitive judgements, and this is evident in a clinical population. However, chapter 9 demonstrated that there was no difference in memory metacognitive efficiency between healthy older adults and ED patients, which suggests that this volumetric variation may be associated with normal ageing as opposed to dementia specific pathology. Alternatively, it is possible that our findings are identifying a neural substrate of very early changes in memory metacognitive efficiency, which are apparent before significant deterioration of performance, in particular with early stages of dementia.

Further, there were a number of significant correlations between the frontal lobe volume: SR was mainly associated with the frontal gyri and SC with the ACC and surrounding areas. Another area of interest was the aPFC, which was positively associated with SR and negatively associated with SC. Further, both BCIS sub-scales had positive neural correlates in common with metacognitive efficiency but these did not overlap, i.e. both self-reflection and memory metacognitive efficiency were associated with volume of the inferior frontal gyrus, and both SC and metacognitive efficiency were associated with areas adjacent to the anterior cingulate volume. These results suggest that neuroimaging methods employed in this study had more statistical power than behavioural methods, and that there may be similar neural regions sub-serving both cognitive insight and metacognitive efficiency in ED patients.

CHAPTER 12

12. DISCUSSION

"Metacognition" is a very broad term referring to thinking about ones' own cognition. This term has been used in the healthy adult cognition literature to investigate introspection of ones' cognitive abilities and its correlates, such as ageing. It has also been used in clinical literature to refer to patients' ability, or lack thereof, to understand and be aware of the various cognitive deficits and symptoms associated with their disorder, also termed "insight into illness". However, current tests of metacognition and assessments of insight are qualitatively different, and to date have not been compared.

This thesis had a number of aims: 1) to investigate the effect of normal ageing on experimentally controlled, objective tasks designed to measure the efficiency of metacognitive judgements on both perception and memory performance, 2) to investigate the cognitive systems and mechanisms underlying both insight into illness and more objective measures of metacognition, and discover whether the two are associated, 3) to investigate how current mood and presence of depression affects insight and metacognitive efficiency, and if this link is more evident in clinical populations compared to healthy controls, and finally, 4) to investigate whether deficits in clinical insight and more objective metacognitive processes are caused by similar cognitive and neural systems across different diagnoses.

12.1 HEALTHY CONTROLS

Previous research into adult metacognitive abilities has focused purely on the ability of adults to think about their own thinking in a number of cognitive domains. This thesis aimed to further this work by additionally looking at metacognitive efficiency in terms of its correlates, such as mood, age and more subjective self-report measures of self-reflection.

12.1.1 *EFFECTS OF AGE ON METACOGNITIVE EFFICIENCY*

Previous evidence was divided when considering the effect of age on metacognitive ability, with some studies suggesting that self-knowledge improves as we age (Doson et al, 2007; Pliske & Mutter, 1996; Vukman, 2005); this was mainly related to a persons' judgement of their general knowledge. A small number of studies utilising Feeling of Knowing (FOK) methodology found no evidence of an age effect (Eakin et al, 2014; Souchay et al, 2007). However much evidence has supported the notion that there is an age related decline associated with metacognitive ability about general memory performance (Huff et al, 2011; Pansky et al, 2009; Weil et al, 2013; Soderstrom et al, 2012), FOK (Cosentino et al, 2011) and Judgements of Learning (JOL ; Tauber & Dunlosky, 2012; Toth et al, 2011). Some have suggested that this is related to memory performance, rather than metacognitive ability itself (Daniels et al., 2009). The current study utilised newly developed methods that control for task performance, and thus produce an objective, experimentally controlled measure of metacognition that is independent of this confound, which has been dubbed "metacognitive efficiency" (Maniscalco and Lau, 2012).

Novel evidence from this study demonstrates that there is a negative effect of age on perceptual metacognitive efficiency across a large span of adulthood. This domain of cognition has received little attention but holds real-world relevance when we consider that perceptual abilities are required to carry out a number of everyday tasks. Indeed, Ross et al (2012) demonstrated that, despite evidence that older drivers were more likely to have driving accidents or violations, they rated their own driving ability as significantly better than objective evidence suggested. Further, evidence from "implicit awareness" research has indicated that adults with disabilities are likely to display adaptive behaviours to deal with their disability, whether it be physical or related to memory, but will not consciously acknowledge that they have a problem (Mograbi & Morris, 2013). These results suggest, therefore, that the weight given to self-ratings made by the older population about their ability to carry out certain tasks, such as driving, should be re-assessed to possibly include an additional rating made by a significant other. Implementation of such a scheme in certain areas of social and health-related tasks may reduce the likelihood of older adults causing accidents and injury to themselves and others, and encourage timely use of services available.

There was no direct correlation between age and memory metacognitive efficiency, which may have been due to lack of power as a result of less participants completing this measure. Post-hoc analyses indicated that there was no significant difference between the effects of age on perceptual and memory metacognitive efficiency, which therefore supported the suggestion of reduced power in this measure. Further investigations with a larger sample size are there required in order to confirm or refute the suggestion that there is an effect of age on memory metacognitive abilities, independent of effects on memory ability. Confirmation of this finding would have practical implications, as we also know there is a robust age related decline in memory ability itself (Stuart-Hamilton, 2012) and thus encouraging older adults to use memory aids in the future may be pragmatic, if individuals may not be aware their memory is getting worse. Implementing such a scheme may help older adults keep their independence and reduce care-giver burden.

Results here also partially support previous work to indicate that different domains of metacognitive ability are associated in healthy adults (McCurdy et al, 2013; Song et al, 2011), although when outliers were removed this result did not remain significant so the strength of the association may not be strong. This behavioural finding implicates at least some underlying common cognitive and perhaps neural basis for metacognitive abilities and self-awareness. This may also impact the understanding of more subtle issues of awareness that may be experienced by patients with localised brain damage (Fleming et al., 2014).

12.1.2 *Effects of mood on metacognitive efficiency*

Novel results were found when investigating the effect of mood on metacognitive efficiency. Memory metacognitive efficiency was negatively associated with increased cognitive symptoms of depression, as measured by the BDI cognitive sub-scale, and this relationship almost reached significance for perceptual metacognitive efficiency. Such results support the notion of depressive realism, where people experiencing low mood show less self-serving bias in relation to self-judgements, which leads to more accurate and "realistic" judgements of one's behaviour.

12.1.3 *Relationship between cognition and metacognitive efficiency*

Though it was suggested there would be significant associations between executive function and metacognitive efficiency, due to their shared association with frontal lobe volume (Fleming & Dolan, 2012; Stuss & Knight, 2013) neither domain of metacognitive efficiency was associated with measures of executive function, unlike previous work using FOKs, (Souchay et al., 2002). However there was a significant relationship between the memory domain of metacognitive efficiency and all measures of memory. This suggests that there is some degree of memory ability required to perform this type of metacognitive judgement, despite memory performance on the task being controlled for using the meta d'/d' calculation (Maniscalco & Lau, 2012).

12.1.4 *Relationship between domains of metacognitive efficiency and awareness*

Initially results supported previous findings that different domains of metacognitive efficiency were associated (McCurdy et al., 2013), however once 3 outliers had been removed (more than 2 standard deviations outside the mean score) this association was no longer significant. A possible explanation is that this may be due to a smaller number of people completing the memory metacognitive task than perceptual metacognitive task, and thus the relationship had less power than previous studies.

Initially a relationship between metacognitive efficiency and measures of awareness (DEX and BCIS) yielded no significant results, however when controlling for age a negative relationship was evident between the self-reflection sub-scale and the memory metacognitive domain, and a positive association with the self-certainty sub-scale and the memory domain approached significance. Though a relationship between metacognitive efficiency and the two BCIS sub-scales was expected, the direction of this association was not. It is therefore suggested that, in healthy adults, self-certainty is not necessarily associated with over-confidence, as in patients samples, but instead a correct appraisal of ones thoughts or behaviour. Further, a larger degree of self-reflection may result in over-thinking and thus metacognitive evaluation of the self is less accurate than automatic responses in these participants.

Further, a gender interaction was evident between the BCIS sub-scales and perceptual metacognitive efficiency, whereby females had a positive relationship between perceptual metacognition and both subscales and males demonstrated negative relationship with both sub-scales. This pattern of results is similar to that observed by Kao et al., (2011) regarding executive function and the BCIS, indicating that there may be some behavioural gender effect influencing the relationship between cognitive functions and cognitive insight.

There was no association between self-rated awareness of dysexecutive symptoms (as measured on the DEX questionnaire) and either domain of metacognitive efficiency, however there was an association between the DEX discrepancy score and memory metacognitive efficiency, where a negative DEX discrepancy score (indicative of participants rating their functioning as worse than their independent-rater), was related to poorer memory metacognitive efficiency, akin to findings from Harty et al. (2013).

Results therefore demonstrate that there is an age related decline in metacognitive efficiency, but not in self-report measures of awareness, indicating the two self-awareness measurements are not directly related. However controlling for age reveals an association between the two. This is the first evidence to suggest that different measures of self-awareness may be related in healthy adults, and indicates that there is a similar cognitive basis for the different domains of awareness in this population.

12.2 First Episode Psychosis

There is a robust body of evidence describing clinical insight in FEP. There is also a growing body of work investigating the qualitative aspect of metacognition in patients with psychotic disorders, and its association with insight and neurocognition, by assessing self- and other-narratives. However, little work has been done to gain objective, experimentally controlled measures of metacognitive function in this clinical group. This thesis aimed to add to the clinical insight and metacognitive literature by carrying out such an investigation and comparing measurement tools and their correlates.

12.2.1 Effects of mood on metacognitive efficiency

A meta-analysis was performed on data measuring depression and cognitive insight in patients with psychosis, which indicated that patients displaying more symptoms of depression had better cognitive insight, driven by the increased capacity to self-reflect. There was no significant relationship with depression and self-certainty. This result was not supported by the data from this experimental study, however non-significant results may have been due to the small patient sample size. There are a number of clinical and ethical implications for the meta-analysis results, mostly centring on interventions designed to improve insight in patients with schizophrenia (Misdrahi, Denard, Swendsen, Jaussent, & Courtet, 2014), as cognitive insight has been identified as an avenue for exploration regarding cognitive behavioural therapy for schizophrenia. Using CBT-like therapy to improve insight should theoretically have an impact on compliance with other forms of treatment, however attempting to improve insight may lead to an increase in symptoms of depression. One suggestion to bypass this potential problem is to develop therapies that attempt to reduce self-certainty bias rather than improve self-reflection. This has also been suggested in the clinical literature to bypass the 'demoralisation effect' of increased depression with improved insight, where Cavelti et al (2012) suggest that treatment targeting insight should focus on helping patients change dysfunctional beliefs and the self, which in turn could encourage patients to take on a positive recovery attitude.

The association between cognitive insight and depression is akin to the association observed between clinical insight and depression (Mintz et al., 2003) and therefore implies that, while the two forms of insight are conceptually separate, they have some similar correlates, and thus are partially related. These findings have led to the conceptualisation of a model of cognitive insight (figure 6.4-1).

12.2.2 Relationship between cognition and metacognitive efficiency

There were no age effects of metacognitive efficiency in this patient group, most likely due to the smaller age range than that of the healthy control group.

Results supported previous work (Lysaker et al., 2005; Morgan & David, 2010) by identifying a negative association between executive function and memory metacognitive efficiency; however this was not the case for perceptual metacognition. A number of patients were not able to complete the task with ~70% correct responses, despite all patients beginning the task. Post-hoc analysis indicated that patients who did complete the task successfully had better executive function on both measures utilised in this study, and also reported less confidence bias in their responses than did the unsuccessful group. There is therefore evidence to suggest executive function is related to the amount of bias patients attribute to their metacognitive ratings; further investigation into this is required before firm conclusions can be drawn.

There was also a significant relationship between memory metacognitive efficiency and all three measures of memory performance (immediate and delayed recall, delayed recognition). Though memory performance on the metacognitive task was controlled for using the Maniscalco and Lau's meta d'/d' calculation, results suggest that some degree of memory ability is required to adequately perform the metacognitive task. Indeed, it may be that, as suggested by Dimaggio & Lysaker (2010), patients with poor memory function may lack the ability to update self-knowledge, and thus will continue to rate their abilities as equal to their premorbid functioning.

There was no significant association between the two domains of metacognitive efficiency, however this is likely due to the low number of patients who successfully completed the perceptual task.

12.2.3 Relationship between domains of metacognitive efficiency and measures of awareness

Whilst the different "concepts" of insight are all referred to as metacognitive processes, evidence suggests that in the FEP group they are not strongly associated with each other, as there was no significant association between any measure of clinical awareness (SAI-E, BCIS or DEX) and either domain of metacognitive efficiency. This finding supports the suggestion that different domains of metacognition are associated but distinct concepts, disrupted in different ways in the FEP population. It further supports the notion that definitions of specific deficits in both insight into illness and awareness should be clearly defined (Marková, 2005), as using such a broad term as "metacognition" in clinical settings may inadvertently imply direct association between two concepts which, in a clinical population, may not necessarily be the case.

12.3 Early-stage Dementia

There is ample evidence to suggest that awareness of memory ability in patients with MCI and AD is poor (Chen et al., 2014; Lopez et al., 1994; Orfei et al., 2010; Roberts et al., 2009; Zanetti et al., 1999), as is awareness of poor executive function (Michon et al., 1994). However, it has been suggested that more objective tests of metacognitive ability are required in order to research metamemory deficits in MCI and AD populations (Cosentino et al., 2007). This study was the first to use methods measuring efficiency (controlling for task performance) as opposed to ability, which has a number of confounds. In addition this was the first study to the author's knowledge to test domains of metacognition other than memory in this clinical population.

12.3.1 *Effects of mood on metacognitive efficiency*

Though previous research has indicated a relationship between mood and memory awareness in MCI and AD, there was no significant association between measures of metacognitive efficiency and either current or clinical mood scores in this ED population.

12.3.2 *Relationship between cognition and metacognitive efficiency*

There was no evidence of an age related effect of metacognitive efficiency in this population. This may be related to the observation that MMSE score was negatively associated with age and positively associated with perceptual metacognitive efficiency score, indicating that as general cognitive ability declined, so did metacognitive efficiency. So in our cross sectional sample selected for presence of cognitive impairment, it was the degree of this impairment, and not age, which drove changes in metacognitive abilities. Further, though the average age in the ED population was ~7 years older than the healthy older adult population, there was no apparent age related cognitive decline in this sample. Longitudinal studies would be useful to indicate whether there is a decline in metacognitive efficiency of ED patients and that it occurs over and above any effects of ageing, perhaps correlating with MMSE score decline.

12.3.3 *Relationship between domains of metacognitive efficiency and measures of awareness*

Due to the low number of patients successfully completing both experimental metacognitive tasks, no conclusions could be drawn regarding the hypothesised association between the two. However exploration of the data suggested there was a positive relationship between perceptual metacognitive efficiency and BCIS self-reflection, supporting the notion that the two forms of self-awareness are related despite measuring different things. Indeed, as stated in section 12.2.3, using the broad term "metacognition" to describe the two processes should be avoided in clinical settings (Marková, 2005). This finding was not replicated in the FEP group, further supporting the notion that the two conditions have different awareness profiles.

12.4 Group comparisons

12.4.1 Healthy adults and patients with FEP and depression

The first group comparison was made between healthy adults under the age of 60, depressed patients and FEP patients. FEP patients scored lower than depressed patients in BCIS self-reflection and self-certainty scores, leading to an overall lower cognitive insight score, supporting previous work indicating that depressed individuals have better insight than FEP patients (Colis et al., 2006). However, healthy adults had lower BCIS self-reflection scores than the FEP group, which led to a lower overcall cognitive insight score. There was also a significant difference between groups on the DEX measure, with depressed patients scoring higher than FEP. The healthy adults scored lowest on both measures of self-awareness, possibly an artefact due to a lack of dysexecutive symptoms and thus no need to acknowledge them and other unusual behaviour, and no need to reflect on their cognitions, as they are "normal". There were significant differences between the three groups on memory metacognitive efficiency, with healthy adults and depressed individuals scoring similarly and close to the "ideal observer" score, whereas the FEP patients performed significantly worse overall despite no difference in task performance between the groups, indicating this group suffers from deficits in metacognition.

12.4.2 Healthy adults and patients with ED

There was no significant difference between healthy older adults over the age of 60 and ED patient groups on awareness measures or metacognitive efficiency. This may suggest that self-awareness and metacognition are spared in earlier stages of dementia and deteriorate at a similar rate to healthy ageing. Similarly it may suggest that some of the healthy older adult group were experiencing a degree of cognitive impairment that has yet to be diagnosed and thus the group spans older age and MCI abilities, and the large range of inclusion in the ED group (MCI and some early stage AD) may have resulted in the two groups' cognitive abilities overlapping and thus no difference coming out. However a comparison of memory and executive function scores between groups indicated there was a significant difference, so the former explanation (sparing of metacognition in ED) is more likely.

12.4.3 Patients with FEP and ED

Finally, the two patient groups were compared. The two groups differed in their awareness ratings, with FEP patients scoring higher on BCIS self-reflectiveness, DEX self-report and SAI-E scales. These results therefore suggest that ED patients have a worse self-report awareness profiles than FEP patients, which supports previous evidence (Gilleen, et al., 2009). However there was no difference between groups on their self-certainty ratings, indicating that neither group is more "overconfident" regarding their self-beliefs. There were no differences between the groups in their metacognitive efficiency, despite a significant difference in age. This therefore suggests that there is a greater degradation in metacognitive efficiency for FEP patients relative to their age compared to ED, who score comparably with their healthy age matched counterparts. One may therefore conclude that, though ED patients appear to be less accurate with their self-reported awareness using questionnaires, FEP patients are worse at judging performance on objective task performance. This finding leads to the conclusion that though both patient groups suffer from problems with their self-awareness, the degree to which domains are affected differs across diagnoses. This suggests that there are a number of processes mediating metacognition and self-awareness in the healthy population, and the different profiles of reduced awareness noted in these patient populations are related to deficits in different mediating processes.

12.5 Neural correlates

In addition to extensive analysis of behavioural measures, this study carried out a pilot imaging study to investigate the neural correlates of metacognitive efficiency and cognitive insight in patients with ED.

The present results indicated that the ACC, which has previously been associated with self-evaluation and monitoring mental activities in healthy adults and awareness of cognitive deficits in patients with dementia (Cosentino, 2014; Ries et al., 2012; Saxe & Offen, 2010), was associated with memory metacognitive efficiency. However, because of the small sample size, results from uncorrected image analyses reported can only be considered exploratory. This region of gray matter has previously been associated with accelerated volumetric reduction in patients with MCI compared to normal ageing (Driscoll et al., 2009), and thus its atrophy may be the substrate of poor awareness in ED patients. However, behaviourally there was no difference between older adults and ED patients, suggesting that imaging studies may hold more power to detect initial and subtle neurodegenerative changes than cognitive testing. Results also indicated that the volume of the right post-central gyrus, part of the parietal lobe, was also associated with memory metacognitive efficiency, which mirrors previous findings from dementia, stroke and lesion studies (Cosentino & Stern, 2005).

A number of frontal areas adjacent to the BA10 area of the aPFC were associated with cognitive insight, where BCIS self-reflection was positively associated with volume of the inferior frontal gyrus, and self-certainty was negatively associated with the middle frontal gyrus. These areas have previously been linked to mediation of metacognitive ability in healthy adults (Fleming et al., 2014; McCurdy et al., 2013), and lesions in this area lead to inferior performance on computerised metacognitive tasks (Fleming et al., 2014), and reduced illness- and self-awareness as associated with reduced gray matter in this region (Cosentino, 2014; Ries et al., 2012). Results therefore further support the suggestion that the aPFC is the main region supporting human self-reflection and introspection (Baird et al., 2013).

A significant correlate of both self-certainty and metacognitive efficiency was volume of areas in the cortical midline structures (CMS), specifically areas adjacent to the anterior cingulate, which has also been consistently associated with metacognitive processes in healthy and patient populations (Ries et al., 2012) and confidence judgements and error detection in healthy adults (Yeung & Summerfield, 2014) and self-reflection (Northoff et al., 2006). As there are a number of frontal and cortical midline structures associated with both metacognitive efficiency and cognitive insight, larger sample sizes may therefore reveal an association between the behavioural measures.

Further, activation in vlPFC and CMS has been associated with self-reflection in patients with schizophrenia (Orfei, 2013; Pu, 2013; Buchy, 2014), indicating that the two patient groups may suffer from problems that arise from deficits in similar neural regions, despite having different awareness profiles.

Analysis of structural correlates in ED patients has therefore indicated that cognitive insight and memory metacognitive efficiency have structural overlaps in the midline and prefrontal regions. This overlap indicates that the concepts have a similar neural basis, but may be behaviourally distinct due to different methods of measurement.

12.6 Conclusions

These studies provide novel evidence about metacognitive processes in healthy and clinical populations. In healthy adults there was an association between low mood and metacognitive efficiency in both the memory and perceptual domains, implicating the effect of cognitive symptoms of depression in better self-appraisal. This also indicates that self-awareness is not uniquely mediated by mood in clinical syndromes. Results have also provided additional evidence to implicate the negative impact of ageing on metacognitive efficiency, and the positive association between different domains of metacognitive efficiency, implicating the need for ‘other’ ratings when older adults are making self-appraisals about their functioning in certain situations. A negative association was found between BCIS self-reflection and memory metacognitive efficiency, as well as an association with discrepancy scores on the DEX. A gender effect was found to mediate the association between scores of cognitive insight and perceptual metacognitive efficiency, which requires further study. These results suggest that, in healthy adults, there is an association between different domains and methods of measuring self-awareness.

Though the conclusions drawn from clinical data are not as firm as those drawn from the healthy population, this study has provided novel evidence in the field of experimentally controlled self-awareness measures in both FEP and ED groups. FEP patients demonstrated an association between memory metacognitive efficiency and both executive function and memory scores, however this was not the case in ED. Neither group demonstrated a significant effect of mood on either domain of metacognitive efficiency. Preliminary findings from ED patients suggest that there is a positive relationship between perceptual metacognitive efficiency and BCIS self-reflection, indicating that different methods of self-reporting awareness of cognition are, at least in part, related in clinical populations. There was also an association between memory metacognitive efficiency and scores on the dysexecutive questionnaire as reported by a significant other, indicating that when assessing objective functioning and behaviour, perhaps a reliable ‘other’ is a more appropriate source of information in clinical groups. However the results do indicate that a brief computerised test would not necessarily be suitable as an objective substitute for clinician or ‘other’ rated measures of awareness in a clinical setting.

The comparison of healthy and clinical groups revealed interesting results on awareness profiles. In the younger groups, there was a clear difference between FEP patients and both depressed and non-depressed adult controls in their memory metacognitive efficiency, where the FEP group were significantly worse at rating their own performance, despite no difference in actual memory task performance. Healthy adults appeared to have a similar level of overall cognitive insight to FEP patients, however the FEP group scored higher on the BCIS self-reflection scale, which was potentially mediated by their higher levels of reported depression, indicating that it may not be possible to differentiate between patients and healthy adults using this scale.

There was no difference between the older adults and ED groups in their memory metacognitive efficiency, implicating a preservation of metacognitive efficiency for task performance in the earlier stages of dementia. Further, there was no difference between the two patient groups on this task, despite a large age difference, indicating that metacognitive efficiency for task performance is relatively more affected in patients with FEP than ED. Conversely, patients with ED were worse at rating their cognitive and behavioural deficits compared to those with FEP, indicating different deficits in self-awareness across diagnoses.

Finally, a pilot MRI study in the ED group indicated that volume of the anterior cingulate and right parietal lobe were positively associated with memory metacognitive efficiency. There were some volumetric correlations with cognitive insight that overlapped with areas associated with metacognitive efficiency, where self-certainty was also associated with anterior cingulate volume. This finding implicates a neural basis for confidence in ones cognitions. Further, prefrontal cortex volume was associated with the BCIS sub-scales; positively with self-reflection and negatively with self-certainty, implying that, though the two measures are associated, it is in a negative direction. This region of the brain has consistently been associated with metacognitive efficiency in domains other than memory; further implicating the two types of self-awareness are associated, at least on a neural level.

In summary, this thesis has demonstrated that metacognition is a multifaceted concept that modulates our self-appraisal at a number of levels. Structural imaging findings support previous work, suggesting that areas of the pre-frontal cortex govern this basic process and are associated with various forms of metacognition identified in the healthy and clinical literature. However, behavioural evidence suggests the relationship is not so clear-cut at a higher cognitive processing level, where the different methods of measuring metacognitive processes become more distinct. This is clear from the observation that different neurocognitive processes, such as memory and executive function, have variable effects on these behaviourally distinct concepts of metacognition. Persistent negative mood states, on the other hand, appear to have a more consistent effect on both clinical and cognitive aspects of metacognition, where lower mood tends to lead to significantly improved self-awareness in healthy adults, and at trend levels in patients. The differential behavioural association between clinical awareness and more objective measures of metacognitive efficiency across populations in this thesis indicates that the umbrella term "metacognition" refers to a number of associated cognitive concepts, but this term should be used with caution in a clinical setting unless stating the context in which it is being used. Further, this suggests that metacognitive training needs to be tailored to the specific type of metacognition that requires improvement to see meaningful changes in awareness.

12.7 Limitations

The main limitation of this study was the low number of patients included in the analyses. Initially it was estimated that a suitable sample size for each group would be 30 participants. That said, those patients that were recruited showed a good range of performance on most of the tasks and scale allowing some cautious conclusions to be drawn. Sample size was a limitation for both behavioural and MRI studies.

There were 3 different insight measures used in the behavioural studies (BCIS, SAI-E and DEX), two of which were originally designed for use with patients with schizophrenia (BCIS and SAI-E), and one was originally designed for use with MCI and AD patients (DEX). Though all measures have been used in more than one clinical population, and the DEX and BCIS are suitable for use in the healthy population (Buchy, Brodeur, & Lepage, 2012), it should be acknowledged that there may be some limitations to the conclusions drawn regarding their associations in different groups. Regarding the BCIS, both healthy controls and ED patients may have found some questions harder to understand, such as those referring to “unusual experiences” (3. Other people can understand the cause of my unusual experience better than I can; 5. Some of my experiences that have seemed very real may have been down to my imagination; 15. My unusual experiences may be due to my being extremely upset or stressed.) Though not all participants queried these items, there were a few for whom these questions required further explanation before they could answer them appropriately. This should be taken into account when interpreting results comparing results across groups.

The use of the WMS raw scores instead of the age adjusted scaled scores may have inflated the difference between groups on their memory ability, as mentioned in Chapter 5. However, the only between groups difference on memory ability identified was that between ED and healthy older adults, which was to be expected as both MCI and AD patients are diagnosed using the MMSE, which is partially dependent on memory ability.

Patients in the ED group were all recruited from the same community patient sample, and all met the same inclusion criteria, however of the 18 included there was a mix of diagnoses, where most had a diagnosis of MCI (12) and a smaller number had a diagnosis of early stage AD (6). The current sample was chosen to ensure that there was a heterogeneity regarding cognitive function, and that the sample was not too impaired when compared to the older adult sample. MCI, in many cases, is seen as a prodromal phase of AD, and a diagnosis is considered a risk factor making patients up to four times more likely to later transition into AD (de Bruijn et al., 2014).

12.8 Future directions

This thesis included a number of studies testing new hypotheses, which were partially confirmed. Larger sample sizes would be useful to test whether results that approached significance reached the threshold in a sample that had more power.

Other interesting avenues of investigation would be to assess metacognitive efficiency before and after metacognitive and insight interventions in patients, to see if efficiency can benefit from CBT-like therapy, and whether interventions are targeting the type of metacognitive process indented.

Further, a longitudinal study to measure the decline of metacognitive efficiency over time after diagnosis in an ED population would indicate at which point metacognitive efficiency is compromised during the course of dementia-related cognitive decline. As mentioned in chapter 8, the inclusion of patients with later stage dementia would also be of interest to investigate the relationship between MMSE and cognitive profile is associated with dementia on a broader diagnostic spectrum.

Evidence from the pilot imaging study suggests that there may be similar neural correlates and deficiencies of self-reflection and metacognitive efficiency in both ED and FEP patients. A study comparing the two populations and their neural correlates relating to both experimental and clinical measures of metacognition would be a useful addition to the literature. Functional imaging could also be utilised to investigate if there is also atypical activations in the regions of interest, such as the aPFC, associated with self-reflection and metacognitive efficiency.

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APPENDIX

5.1 MEMORY METACOGNITION WORD LISTS

Words used in the memory metacognition task come from a randomly chosen list of 50 words (listed below). Three are chosen at random by the program for the 'learning' phase of the task. In each of the three test phases, one "learned/old" word is presented alongside a "new" word, taken from a new, randomly selected, list of words.

SWEAT	ANIMAL	BUTTON	SUGAR	THIEF	SHRUB
CHAIR	BREAST	SLOPE	TUNE	YAWN	DAYLIGHT
ROCK	TULIP	ESSAY	LENS	TABLE	CORD
SOAP	WEAPON	STAR	SNAP	BANANA	PAINT
HEAD	TUCK	SKIRT	TREE	MINE	BATH
POLLEN	GLASS	FROG	SUNBURN	ALERT	GARLIC
BATTLE	HERB	TRASH	SNOW	TALK	UNIFORM
ARMOUR	FLOOD	HARP	SUITE	FEAST	FIGHT
HORN	SALARY	COLD	TENNIS	LIGHT	SALT
WHEEL	CHAIN	HOLIDAY	JELLY	HIND	BLUSH
HAIL	RABBIT	SOCK	TORTURE	FROST	STREET
FOOTBALL	CHEEK	MOUNTAIN	CELL	SLIP	STEAM
HEEL	BACK	CRAWL	SMOKE	SNEEZE	DANCER
TEETH	CLOCK	COCKTAIL	ROAD	MONKEY	SKIN
RULER	WHITE	FLAG	HUSBAND	FRONT	MOUSE
WOUND	CEMENT	STUDENT	ENTRANCE	FIRE	SKUNK
BANKER	SWEEP	HUNTER	SHOOT	SEED	DAMAGE
FLOCK	MESSAGE	SHEEP	ADULT	SHADOW	OCEAN
PHONE	SUNLIGHT	LINE	BEDROOM	SPICE	PEDAL
JUICE	FACTORY	PRIZE	GASP	BEAN	WATCH
FAINT	PANTS	ACCIDENT	PEACH	CHIEF	GOLF
SOFT	ROLL	HALL	DOOR	ITCH	FLAME
PRINCESS	EVENING	MILK	BLOOD	AUNT	NECK
COUSIN	SANDAL	LIZARD	OLIVE	SCISSORS	STOMACH
LAUGH	WIRE	TENT	FLOAT	LIVER	GUIDE
MASH	ENVELOPE	PARCEL	FILM	MARCH	COFFEE
CONE	SHORE	CATTLE	SWIM	BUBBLE	BADGE
ROOT	SNORT	SPEECH	CABINET	MOON	MUSIC
BROTHER	POCKET	SNAKE	WHISTLE	SWARM	TOUCH
PRISONER	TEXT	DUMMY	TOBACCO	COVER	FABRIC
DESK	ANCHOR	TWIST	BOSS	CHILDREN	SHOVEL
INFANT	GRAVY	VEHICLE	SPOON	CARD	WIZARD
THORN	DRILL	COMFORT	WINK	WHISPER	GRAVE
MORNING	KNEE	SPOOK	CHICKEN	CABLE	SLAVE
BULLET	MATCH	STATE	SOUND	HAIR	BURN
HOOK	ECHO	BRAIN	CRANK	SUIT	CITY
ROOM	JUDGE	HERO	PUPIL	MARKET	TRUCK
FLUTE	TANK	SLICE	MAGNET	RUBBER	ELEPHANT
SOIL	DIVE	STALK	GLARE	GIFT	WALK
BOARD	PLAIN	FILE	DRUG	HOWL	EDGE
SISTER	BOMB	BASKET	SKATE	BRAKE	FOREHEAD
KITE	POSTER	HOSE	WORM	WOOD	MIRROR
PORCH	SHIELD	KISS	FEVER	UMPIRE	DRUM
FLUSH	WORLD	ACHE	SCENT	HOUSE	INSECT
PEST	ONION	BLANKET	CIGAR	PEOPLE	PAINTER
SPARK	BLUE	LETTER	DRINK	KNOB	BEER
SUDS	ZIPPER	SUNSET	PREY	SPRINT	FISH
PUPPY	POETRY	POLE	BUCKLE	DUCK	DIAMOND
BOOK	THUNDER	MEAL	TEAM	CUCUMBER	KNIFE

ATHLETE	SAIL	BABY	FIRM	LANE	FIGURE

ENEMY	HONEY	STOVE	FOOT	BIRD	WHEAT
DATE	ROCKET	STAIN	SPIDER	DEEP	PORK
PILLOW	CANDLE	TWIG	LOBBY	BROOM	MOSS
DIRT	FRAME	HELMET	PASTURE	SOUP	LAMP
BASEMENT	DRAW	GRAPH	DINNER	STRING	STICK
PEAR	VASE	ORANGE	MOTH	WORKER	CITIZEN
SHOE	MOVIE	STONE	COUNTRY	CLAW	SPRAY
CABBAGE	TOAD	PILL	MAIL	SHOWER	TOMB
FROWN	APPLE	ROBBER	MUCUS	CLOWN	FIREWOOD
DRESS	OFFICE	WAIST	SHOUT	SEAT	BUMP
SHIP	BEAST	LUNG	ROPE	NEST	STABLE
KNIGHT	HAND	HOTEL	TRIANGLE	SMELL	THUMB
CLOTHING	STRAW	MOLE	EAGLE	PUDDLE	DOVE
WING	SLEEVE	BRICK	GATE	HOCKEY	JEWEL
FLESH	MOTHER	WORK	CROSS	DEER	HAZE
OWNER	DISPLAY	POTATO	MACHINE	WITCH	FAIR
POOL	COIN	BUCKET	RECORD	RADIO	POND
RIDDLE	TEACHER	BRANCH	NAVY	SCHOOL	SILVER
BALL	SCRATCH	HERRING	WATER	STEEL	REPORT
BRIDGE	SOFA	DAIRY	LESSON	LAUGHTER	TRAIN
CURVE	HORSE	CROW	HEART	SONG	BUTTER
UMBRELLA	CANAL	DOLLAR	NAME	NEEDLE	CHEST
OBJECT	TOMATO	FOOTSTEP	RICE	CLUB	NECKLACE
CORK	HAMMER	GREEN	SMALL	SPRING	GRIP
STORY	ROUGH	CLOUD	CAMEL	TAIL	PEARL
CRAB	NOODLE	DOCTOR	STEP	PIMPLE	DAWN
FENCE	FOREST	GRATE	GLUTTON	GOWN	CAVE
CHALK	VILLAGE	PIANIST	ROAR	BEAR	BOIL
WRAP	MEDICINE	PENCIL	FATHER	LAWN	SHOP
MATTRESS	COSTUME	CLARINET	RING	MIST	GIANT
ROSE	WITNESS	STING	BISCUIT	POINT	GOLD
WALLET	FUSE	TUMBLE	LIMB	HEAT	TOWER
UNCLE	THREE	MAZE	STORM	ROUND	VEIL
DRAIN	COACH	TOOL	CIRCLE	BOWL	SHEET
TOOTH	FEET	LEATHER	WOMB	GORILLA	NATURE
GLOVE	COUCH	OYSTER	TOWN	SALAD	BLOUSE
ELBOW	CORNER	STAIR	WHIP	FRICTION	LOCKER
CAGE	SHIRT	DRIVER	TROLLEY	GALLERY	RIVER
TRAVEL	GOAL	SLIDE	PONY	PUDDING	FERRY
STEAK	FLEA	SEWER	THREAD	BIRTH	FOAM
HOOD	HOOF	POPE	TIGER	LANTERN	PORTRAIT
TUNNEL	STAND	SEAL	ISLAND	MALE	MAGAZINE
BOAT	GANG	BASIN	GIRL	LIBRARY	FRIEND
EARTH	ANGLE	MATERIAL	BOTTLE	PILE	SINGER
FLOOR	LINKS	PURSE	LAND	HOSPITAL	ATOM
BERRY	POISON	BONE	IRON	HUNGER	VISITOR
SPIKE	FLOWER	SPONGE	CROWN	FOREARM	OFFICER
BALLOON	CURFEW	WOOL	SHOULDER	ARMY	FOIL

PLANE	TOAST	TASK	PLANT	VEIN	VINEGAR
RAKE	RAIN	AUDIENCE	GUARD	TAILOR	FAMILY

TOURIST	SUBJECT	WOMAN	CLAY	LEAF	WHALE
SWEET	PLATE	TRIP	KICK	CHAMPION	SHIVER
BODY	LINK	NAIL	CONCRETE	BOUNDARY	PARTY
TEAR	WALRUS	BREATH	CARROT	THROAT	BENCH
COTTAGE	WRITING	BOOT	RENT	LAMB	SEASON
COMPANY	BUSH	PACKAGE	MATE	DISEASE	SLIT
SCALE	LIAR	CART	FARM	GROUP	BLISTER
NATION	HOME	REBEL	AVENUE	JAIL	TUBE
KITTEN	DIAL	OUTFIT	SNAIL	LABOUR	BLOSSOM
LAKE	PICK	SHOW	CASE	BRAT	LECTURE
JUMP	RAID	TRIAL	PUZZLE	LETTUCE	TRUNK
NAPKIN	CREAM	WHIRL	DIET	TIRE	CHOP
SHRIEK	SCAR	ENGINE	WALL	FACE	LILY
BUNCH	DRIZZLE	PLANET	CLOTH	DENTIST	ALLEY
TURTLE	CREW	GRIZZLY	SORE	CANE	PAPER
POLO	LAWYER	BRASS	CARPET	TAPE	VOLCANO
HIDE	SILK	CUSTOMER	COLUMN	WINTER	LAUNDRY
CAMP	BEAM	ARTICLE	MEDAL	DANCE	LOOP
GROUND	TASTE	HAWK	BEAVER	LEAK	BEGGAR
SKETCH	CURB	SPEAR	JACKET	SQUIRREL	BLONDE
PASTE	SEAM	MISSILE	VEAL	MOUTH	VINE
LORD	WINDOW	TOILET	LIQUID	SWORD	THROW
CORE	VOICE	CHERRY	BEETLE	HARE	PRISON
LOOT	PUNCH	WIFE	LEADER	RACE	CREATURE
CIRCUS	CROWD	FOUNTAIN	SHELL	TICKET	PIANO
PASSAGE	NOTE	STUMBLE	WIND	VIOLIN	ALCOHOL
CHANNEL	STAFF	LEAD	AUTHOR	PRINCE	WASH
PARTNER	MONEY	BORDER	ANKLE	CANDY	GLITTER
WOLF	SHARK	DUSK	DESIGN	WASTE	SUNSHINE
NURSE	COURT	PEEL	SIGN	CEREAL	QUEEN
GRAPE	TIDE	TEST	FLAVOUR	SAUCE	FALL
SELF	ROOF	PLUG	DART	PIPE	BARN
MURDER	STATUE	SQUINT	ENGINEER	YOUTH	PEPPER
CHILD	MOISTURE	COTTON	BANK	CORN	TRACK
LEMON	BELLY	DISASTER	ARTIST	BEACH	HILL
WAVE	SLEEP	CAKE	BAND	PLANK	DOLL
SKULL	JOURNAL	SQUARE	WELL	BLIND	STORE
POST	BREAD	BELT	POET	MUSTARD	GOAT
INJURY	CEILING	OVEN	NERVE	SLAP	POWDER
COLLAR	GLOBE	LION	LOCK	KNUCKLE	COAT
TRAIL	FLASH	BEEF	LOBSTER	PARK	FORK
SLIME	BRUSH	KETTLE	CHIN	COAST	SIGNAL
GRASS	CALF	SPINACH	BLOCK	LADY	PLAY

RIFLE	ARROW	MANSION	NIGHT	WHISKER	PICTURE
FOOD	CASH	DUST	HOLE	PHYSICS	RIBBON
SCREAM	SOCCER	REPTILE	SWAMP	FRUIT	HOBBY
NEWS	LIFT	YOKE	HUNT	PUMP	TRUMPET
SOLE	METAL	CHURCH	WIDOW	MASTER	SMILE
SOLDIER	BURIAL	FANG	SACK	COOK	WEATHER
BARK	POLL	BOLT	WINE	SHOT	TONGUE

5.2 Visual Analogue Scale

Please mark on the line how happy you are feeling right now:

1 Very Sad 10 Very Happy

5.3 BECK DEPRESSION INVENTORY - II

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement that you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including item 16 (changes in sleeping pattern) or item 18 (changes in appetite).

1. Sadness

0 I do not feel sad.
1 I feel sad.
2 I am sad all the time.
3 I am so sad and unhappy that I can't stand it.

2. Pessimism

0 I am not discouraged about my future.
1 I feel more discouraged about my future than I used to be.
2 I do not expect things to work out for me.
3 I feel my future is hopeless and will only get worse.

3. Past Failure

0 I do not feel like a failure.
1 I feel I have failed more than I should have.
2 As I look back, I see a lot of failures.
3 I feel I am a total failure as a person.

4. Loss of Pleasure

0 I get as much pleasure as I ever did from the things I enjoy.
1 I don't enjoy things the way I used to.
2 I don't get very little pleasure from the things I used to enjoy.
3 I can’t get any pleasure from the things I used to enjoy.

5. Guilty Feelings

0 I don't feel particularly guilty
1 I feel guilty over many things I have done or should have done.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6. Punishment feelings

0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.

7. Self-Dislike
0 I feel the same about myself as ever.
1 I have lost confidence in myself.
2 I am disappointed with myself.
3 I dislike myself.

8. Self-Criticalness
0 I don't criticise or blame myself more than usual.
1 I am more critical of myself than I used to be.
2 I criticise myself for all my faults.
3 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes
0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10. Crying
0 I don't cry any more than usual.
1 I cry more now than I used to.
2 I cry over every little thing.
3 I feel like crying, but I can’t.

11. Agitation
0 I am no more restless or wound up than usual.
1 I feel more restless or wound up than usual.
2 I am so restless or agitated that it’s hard to stay still.
3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest
0 I have not lost interest in other people or activities.
1 I am less interested in other people or things than before.
2 I have lost most of my interest in other people or things.
3 It’s hard to get interested in anything.

13. Indecisiveness
0 I make decisions about as well as I ever could.
1 I put off making decisions more than I used to.
2 I have greater difficulty in making decisions more than I used to.
3 I can't make decisions at all anymore.

14. Worthlessness
0 I don't feel I am worthless.
1 I don’t consider myself as worthwhile and useful as I used to.
2 I feel more worthless as compared to other people.
3 I feel utterly worthless

15. Loss of Energy

0 I have as much energy as ever.
1 I have less energy than I used to.
2 I don't have enough energy to do very much.
3 I don't have enough energy to do anything.

16. Changes in sleeping pattern

0 I have not experiences any change in my sleeping pattern.
1a I sleep somewhat more than usual.
1b I sleep somewhat less than usual.
2a I sleep a lot more than usual.
2b I sleep a lot less than usual.
3a I sleep most of the day.
3b I wake up 1-2 hours early and can't get back to sleep.

17. Irritability

0 I am no more irritable than usual.
1 I am more irritable than usual.
2 I am much more irritable than usual.
3 I am irritable all the time.

18. Changes in appetite

0 I have not experiences any change in my appetite.
1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.
2a My appetite is much less than usual.
2b My appetite is much greater than usual.
3a I have no appetite at all.
3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.
I can't concentrate as well as usual.
It's hard to keep me mind on anything for very long.
I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.
I get more tired or fatigued more easily than usual.
I am too tired and fatigued to do a lot of the things I used to do.
I am too tired and fatigued to do most of the things I used to do.

21. Loss of interest in Sex

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

Total: ________________

5.4 Beck Cognitive Insight Scale

Instructions: This questionnaire consists of 15 statements. Please read each statement carefully, and then decide if you 1 - Do not agree at all, 2 - Agree slightly, 3 - Agree a lot or 4 - Agree completely. Circle the number under the statement that you have picked. Be sure that you do not choose more than one statement for any group.

	Do not agree at all	**Agree slightly**	**Agree a lot**	**Agree completely**
1. At times, I have misunderstood other people's attitudes towards me.	1	2	3	4
2. My interpretations of my experiences are definitely right.	1	2	3	4
3. Other people can understand the cause of my unusual experiences better than I can.	1	2	3	4
4. I have jumped to conclusions too fast.	1	2	3	4
5. Some of my experiences that have seemed very real may have been down to my imagination.	1	2	3	4
6. Some of the ideas I was certain were true turned out to be false.	1	2	3	4
7. If something feels right, it means it is right.	1	2	3	4
8. Even though I feel strongly that I am right, I could be wrong.	1	2	3	4
9. I know better than anyone else what my problems are.	1	2	3	4
10. When people disagree with me, they are generally wrong.	1	2	3	4
11. I cannot trust other people's opinion about my experiences.	1	2	3	4
12. If somebody points out that my beliefs are wrong, I am willing to consider it.	1	2	3	4
13. I can trust my own judgement at all times.	1	2	3	4
14. There is often more than one possible explanation for why people act the way they do.	1	2	3	4
15. My unusual experiences may be due to my being extremely upset or stressed.	1	2	3	4

5.5 Dysexecutive Questionnaire

Subject Rater

This questionnaire looks at some of the difficulties that people sometimes experience. We would like you to read the following statements, and rate them on a five-point scale. Please read each statement carefully, and then decide how often this statement applies to you. Circle the number under the statement that you have picked. Be sure that you do not choose more than one statement for any group.

1. **I have problems understanding what other people mean unless they keep things simple and straightforward.**

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

2. **I act without thinking, doing the first thing that comes to mind.**

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

3. **Sometimes I talk about events or details that never actually happened, but I believe they happened.**

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

4. **I have difficulty thinking or planning for the future.**

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

5. **Sometimes I get over-excited about things and can be a bit ‘over the top’ at these times.**

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

6. **I get events mixed up with each other, and get confused about the correct order of events.**

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

7. **I have difficulty realising the extent of my problems and am unrealistic about the future.**

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

8. **I am lethargic or unenthusiastic about things.**

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

9. **I do or say embarrassing things when in the company of others.**

0	1	2	3	4

Never Occasionally Sometimes Fairly Often Very Often

10. I really want to do something one minute, but couldn't care less about it the next.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

11. I have difficulty showing emotion.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

12. I lose my temper at the slightest thing.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

13. I am unconcerned about how I should behave in certain situations.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

14. I find it hard to stop repeating saying or doing things once started.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

15. I tend to be very restless and 'can't sit still' for any length of time.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

16. I find it difficult to stop doing something even if I know I shouldn't.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

17. I will say one thing, but do something different.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

18. I find it difficult to keep my mind on something, and am easily distracted.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

19. I have trouble making decisions, or deciding what to do.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

20. I am unaware or unconcerned about how others feel about my behaviour.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

Independent Rater

This questionnaire looks at some of the difficulties that people sometimes experience. We would like you to read the following statements, and rate them on a five-point scale according to your experience of…………………………………*(subject).* Please read each statement carefully. Circle the number under the statement that you have picked. Be sure that you do not choose more than one statement for any group.

1. Has problems understanding what other people mean unless they keep things simple and straightforward.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

2. Acts without thinking, doing the first thing that comes to mind.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

3. Sometimes talks about events or details that never actually happened, but he/she believes they happened.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

4. Has difficulty thinking or planning for the future.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

5. Sometimes gets over-excited about things and can be a bit 'over the top' at these times.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

6. Gets events mixed up with each other, and get confused about the correct order of events.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

7. Has difficulty realising the extent of their problems and is unrealistic about the future.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

8. Seems lethargic or unenthusiastic about things.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

9. Does or says embarrassing things when in the company of others.

0	1	2	3	4

Never	Occasionally	Sometimes	Fairly Often	Very Often

10. Really wants to do something one minute, but couldn't care less about it the next.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

11. Has difficulty showing emotion.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

12. Loses his/her temper at the slightest thing.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

13. Is unconcerned about how he/she should behave in certain situations.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

14. Finds it hard to stop repeating saying or doing things once started.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

15. Tends to be very restless and 'can't sit still' for any length of time.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

16. Finds it difficult to stop doing something even if he/she knows they shouldn't.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

17. Will say one thing, but do something different.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

18. Finds it difficult to keep their mind on something, and is easily distracted.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

19. Has trouble making decisions, or deciding what to do.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

20. Is unaware or unconcerned about how others feel about his/her behaviour.

0	1	2	3	4
Never	Occasionally	Sometimes	Fairly Often	Very Often

5.6 Schedule for the Assessment of Insight - Extended

1. "Do you think you have been experiencing any emotional or psychological changes or difficulties?"

often (thought present most of the day, most days) = 2

sometimes (thought present occasionally)

never (ask why doctors / others think so)

If brief write verbatim reply, otherwise summarise response. Please add explanatory comments if appropriate.

2. "Do you think this means there is something wrong with you?" (For example, a nervous condition). *If previous answer was "never" or "no" ask ; "If the doctor(s) and/or others think you have been experiencing emotional or psychological changes or difficulties do you think there must be something wrong with you even though you don't feel it yourself?"*

often (thought present most of the day, most days) = 2

sometimes (thought present occasionally)

never (ask why doctors / others think so)

If brief write verbatim reply, otherwise summarise response. Please add explanatory comments if appropriate.

3. "Do you think your condition amounts to a mental illness or mental disorder?"

often (thought present most of the day, most days) = 2

sometimes (thought present occasionally)

never (ask why doctors / others think so)

If brief write verbatim reply, otherwise summarise response. Please add explanatory comments if appropriate.

4. "How do you explain your condition /disorder /illness?" *Reasonable account given based on plausible mechanisms* (appropriate given social, cultural and educational background, e.g. excess stress, chemical imbalance, family history, etc.) = 2 *Confused account, or overheard explanation without adequate understanding or "don't know"* = 1 *Delusional or bizarre explanation* = 0
If brief write verbatim reply, otherwise summarise response. Please add explanatory comments if appropriate.

If positive score on items 1,2, and 3, proceed to 5, otherwise go to item 6.

5. "Has your nervous/emotional /psychological /mental /psychiatric condition (use patient's term) led to adverse consequences or problems in your life? (For example, conflict with others, neglect, financial or accommodation difficulties, irrational, impulsive or dangerous behaviour). *Yes* (with example) = 2 *Unsure* (cannot give example or contradicts self) = *No*
If brief write verbatim reply, otherwise summarise response. Please add explanatory comments if appropriate.

6. "Do you think your ... condition (use patient's term) or the problem resulting from it warrants (needs) treatment?" *Yes* (with plausible reason) = 2 *Unsure* (cannot give example or contradicts self) = *No*
If brief write verbatim reply, otherwise summarise response. Please add explanatory comments if appropriate.

7. Pick the most prominent symptoms up to a maximum of 4. Then rate awareness of each symptom out of 4 as below. (Interviewer to assess which symptoms to rate from previous interviews e.g. highest scoring on BPRS and/or from patient's current presentation).

Examples:

"Do you think that the belief ... is not real / not really happening (could you be imagining things)?"

"Do you think the 'voices' you hear are actually real people talking, or is it something arising from your own mind?"

"Have you been able to think clearly, or do your thoughts seem mixed up / confused? Is your speech jumbled?"

"Would you say you have been more agitated / overactive / speeded up / withdrawn than usual?"

"Are you aware of any problem with attention / concentration / memory?"

"Have you a problem with doing what you intend / getting going / finishing tasks / motivation?"

Symptom 1 - type:		Symptom 2 - type:	
rating	rating	rating	rating

Definitely (full awareness)

Probably (moderate awareness) = 3

Unsure (sometimes yes, sometimes no) = 2

mean

Possibly (slight awareness)

Absolutely not (no awareness) =

If brief write verbatim replies, otherwise summarise responses. Please add explanatory comments if appropriate.

8. For each symptom rated above (up to a maximum of 4), ask patient ... "How do you explain ... (false beliefs, hearing voices, thoughts muddled, lack of drive etc.)?"

Symptom 1

Symptom 3

Symptom 2

Symptom 4

☐ ☐ ☐ ☐

Part of my illness

Due to nervous condition

mean

Reaction to stress / fatigue

☐

Unsure, maybe one of the above

Can't say, or delusional / bizarre explanation = 0

If brief write verbatim reply, otherwise summarise response. Please add explanatory comments if appropriate.

9. “How do you feel when people do not believe you? (when you talk about ... delusions or hallucinations).” *That’s when I know I’m sick* = 4 *I wonder whether something’s wrong with me* = 3 *I’m confused and I don’t know what to think* = 2 *I’m still sure despite what others say* = 1 ☐ *They’re lying* = 0
If brief write verbatim reply, otherwise summarise response. Please add explanatory comments if appropriate.

Please turn to page 8 after interview and fill in grid as appropriate.

Compliance to treatment/therapy/medication - patient's primary nurse to rate following three items (A-C).

A. How does patient accept treatment (includes passive acceptance)?

Often (may rarely question need for treatment) = 2

sometimes (may occasionally question need for treatment) = 1

never (ask why) -

Please add explanatory comments if appropriate.

B. Does patient ask for treatment unprompted?

Often (excludes inappropriate request for medication etc.) = 2

Sometimes (rate here if forgetfulness/disorganization leads to occasional requests only) = 1

Never (ask why doctors / others think so) = 0

Please add explanatory comments if appropriate.

C. Summary of compliance to treatment/therapy/medication.

Complete refusal	=	1
Partial refusal (e.g. refusing depot drugs or accepting only the minimum dose)	=	2
Reluctant acceptance (accepting only because treatment is compulsory or questioning the need for treatment often e.g. every two days)	=	3
Occasional reluctance about treatment (questioning the need for treatment once a week)	=	4
Passive acceptance	=	5
Moderate participation (some knowledge of and interest in treatment and no prompting needed to take the drugs)	=	6
Active participation (ready acceptance, and taking some responsibility for treatment)	=	7

Please add explanatory comments if appropriate.

	Patient	Primary Nurse
ID		
Date of interview		
Time started		
Time finished		
Rater ID		

Score summary

1. ☐
2. ☐
3. ☐
4. ☐
5. ☐
6. ☐
7. ☐ (mean)
8. ☐ (mean)
9. ☐

Sub total ☐

A. ☐

B. ☐ **NB: Item C is not combined with other scores**

Total ☐ **Item C.** ☐

General comments/observations

2. Logical Memory I

Date of issue: 04/04/2013
Version number: 1

SCORING RULES

Story A

Anna Thompson of South London, employed as a cook in a school canteen, reported at the police station that she had been held up on the High Street the night before and robbed of fifty-six pounds. She had four small children, the rent was due, and they had not eaten for two days. The police, touched by the woman's story, made up a collection for her.

	Score 0 or 1		
Story A	Story Unit	Thematic Unit	Scoring Criteria
Anna			*Anna* or variant of the name
Thompson			*Thompson* is required
of South			*South* (in any context)
London,			*London* (in any context)
			Indication of a main character who is female
employed			indication that she held a job
as a cook			*cook* or some form of the word is required
in a school			*school* is required
canteen,			*canteen* is required
			Indication that main character is employed or is working
reported			indication that a formal statement was made to someone in authority (in any context)
at the police			*police* (in any context)
station			*station* (in any context) or a word or phrase denoting a police station
that she had been held up			indication that she had been held up (i.e., gunpoint or knife)
on the High Street			*the High Street* (in any context)
the night before			indication that the hold-up occurred the previous night
and robbed			indication that a robbery took place
of fifty-six pounds.			indication that an amount of money greater than £49 but less than £60 was taken from her
			Indication that main character reported she was robbed
She had four			*four* is required together with an indication that the children were hers
small children,			*children* or a synonym is required
			Indication that main character had children
the rent was due,			a phrase indicating that the rent was due
and they had not eaten			indication that her children or the family were without food
for two days.			*two days* is required, or a phrase meaning about two days
			Indication that characters were in need or required assistance
The police,			a word or phrase signifying one or more members of the police (in any context)
touched by the woman's story,			indication that her story evoked sympathy
			Indication that the police felt sympathy for the woman
made up a collection			a phrase indicating that money was collected
for her.			indication that the money collected was for her or her children
			Indication that the police directly responded to her need

Story A Recall Unit Score Range 0 to 25

Story A Thematic Unit Score Range 0 to 7

Story B–1st Recall

2. Logical Memory I *(continued)*

At 6:00 on Monday evening, Joe Grant of Liverpool was watching television as he dressed to go out. A weather report interrupted the programme to warn that thunderstorms would move into the area within the next two to three hours and remain until morning. The announcer said the storm could bring hail and up to four inches of rain and cause the temperature to drop by fifteen degrees. Joe decided to stay home. He took off his coat and sat down to watch old films.

	Score 0 or 1		
Story B — 1st Recall	Story Unit	Thematic Unit	Scoring Criteria
At 6:00			*6:00* is required
on Monday			*Monday* is required
evening,			*evening* (in any context)
Joe			*Joe* or variant of the name
Grant			*Grant* is required
of Liverpool			*Liverpool* is required
			Indication of a main character who is male
was watching television			indication that he was watching/listening to the television
as he dressed			indication that he was getting dressed
to go out.			indication that he was going out
			Indication that the character was preparing to leave
A weather report			indication that there was an announcement about weather
interrupted the programme			indication of a break in the regularly scheduled programme
			Indication of a weather announcement
to warn that thunderstorms			indication that there was a warning about a storm
would move into the area			indication that the storm was coming
			Indication of a storm moving into the area
within the next 2 to 3 hours			a phrase meaning about 2 or 3 hours
and remain until morning.			indication that the storm would stay until morning
			Indication of storm duration
The announcer said			indication that someone was reporting about a storm
the storm could bring hail			indication that hail was possible
and up to 4 inches			*4 inches* is required
of rain			*rain* is required
and cause the temperature to drop			indication that the temperature would drop or decrease
by 15 degrees.			a relative decrease of 15 degrees is required
			Indication of storm's activity
Joe decided to stay home.			indication that he decided to stay home
			Indication that the character decided to stay in
He took off his coat			indication that he took off outer clothing
and sat down			indication that he was sitting down
to watch old films.			indication of viewing films is required
			Indication that the character decided to watch a film or TV

Story B — 1st Recall Unit Score Range = 0 to 25

Story B — 1st Recall Thematic Unit Score Range = 0 to 8

1st Recall Total Score Calculation

Story A Recall Unit Score Range = 0 to 25 + Story B —1st Recall Unit Score Range = 0 to 25 = 1st Recall Total Score Range = 0 to 5(

Story B-2nd Recall **2. Logical Memory I** *(continued)*

At 6:00 on Monday evening, Joe Grant of Liverpool was watching television as he dressed to go out. A weather report interrupted the programme to warn that thunderstorms would move into the area within the next two to three hours and remain until morning. The announcer said the storm could bring hail and up to four inches of rain and cause the temperature to drop by fifteen degrees. Joe decided to stay home. He took off his coat and sat down to watch old films.

	Score 0 or 1		
Story B — 2nd Recall	Story Unit	Thematic Unit	Scoring Criteria
At 6:00			*6:00* is required
on Monday			*Monday* is required
evening,			*evening* (in any context)
Joe			*Joe* or variant of the name
Grant			*Grant* is required
of Liverpool			*Liverpool* is required
was watching television			indication that he was watching/listening to the television
as he dressed			indication that he was getting dressed
to go out.			indication that he was going out
A weather report			indication that there was an announcement about weather
interrupted the programme			indication of a break in the regularly scheduled programme
to warn that thunderstorms			indication that there was a warning about a storm
would move into the area			indication that the storm was coming
within the next 2 to 3 hours			a phrase meaning about 2 or 3 hours
and remain until morning.			indication that the storm would stay until morning
The announcer said			indication that someone was reporting about a storm
the storm could bring hail			indication that hail was possible
and up to 4 inches			*4 inches* is required
of rain			*rain* is required
and cause the temperature to drop			indication that the temperature would drop or decrease
by 15 degrees.			a relative decrease of 15 degrees is required
Joe decided to stay home.			indication that he decided to stay home
He took off his coat			indication that he took off outer clothing
and sat down			indication that he was sitting down
to watch old films.			indication of viewing films is required

Story B—2nd Recall Unit Score Range = 0 to 25

Story B— 2nd Recall Thematic Unit Score Range = 0 to 8

Recall Total Score Range = 0 to 75

Thematic Total Score Range = 0 to 23

Learning Slope Calculation

Story B—2nd Recall Unit Score − Story B—1st Recall Unit Score = Learni… Ra… -25 t…

12. Logical Memory II

Recall

ADMINISTER 25–35 MINUTES AFTER LOGICAL MEMORY I

RECORDING
[illegible] unit [illegible] verbatim [illegible]

SCORING RULE
[illegible]

Reminder Given? ☐ Yes ☐ No

	Score 0 or 1		
Story A	**Story Unit**	**Thematic Unit**	**Scoring Criteria**
Anna			*Anna* or variant of the name
Thompson			*Thompson* is required
of South			*South* (in any context)
London,			*London* (in any context)
			Indication of a main character who is female
employed			indication that she held a job
as a cook			*cook* or some form of the word is required
in a school			*school* is required
canteen,			*canteen* is required
			Indication that main character is employed or is working
reported			indication that a formal statement was made to someone in authority (in any context)
at the police			*police* (in any context)
station			*station* (in any context) or a word or phrase denoting a police station
that she had been held up			indication that she had been held up (i.e., gunpoint or knife)
on the High Street			*the High Street* (in any context)
the night before			indication that the hold-up occurred the previous night
and robbed			indication that a robbery took place
of fifty-six pounds.			indication that an amount of money greater than £49 but less than £60 was taken from her
			Indication that main character reported she was robbed
She had four			*four* is required together with an indication that the children were hers
small children,			*children* or a synonym is required
			Indication that main character had children
the rent was due,			a phrase indicating that the rent was due
and they had not eaten			indication that her children or the family were without food
for two days.			*two days* is required, or a phrase meaning about two days
			Indication that characters were in need or required assistance
The police,			a word or phrase signifying one or more members of the police (in any context)
touched by the woman's story,			indication that her story evoked sympathy
			Indication that the police felt sympathy for the woman
made up a collection			a phrase indicating that money was collected
for her.			indication that the money collected was for her or her children
			Indication that the police directly responded to her need

Story A Recall Unit Score
Range = 0 to 25

Story A Thematic Unit Score
Range = 0 to 7

12. Logical Memory II *(continued)*

Reminder Given? ☐ Yes ☐ No

	Score 0 or 1		
Story B	Story Unit	Thematic Unit	Scoring Criteria
At 6:00			*6:00* is required
on Monday			*Monday* is required
evening,			*evening* (in any context)
Joe			*Joe* or variant of the name
Grant			*Grant* is required
of Liverpool			*Liverpool* is required
			Indication of a main character who is male
was watching television			indication that he was watching/listening to the television
as he dressed			indication that he was getting dressed
to go out.			indication that he was going out
			Indication that the character was preparing to leave
A weather report			indication that there was an announcement about weather
interrupted the programme			indication of a break in the regularly scheduled programme
			Indication of a weather announcement
to warn that thunderstorms			indication that there was a warning about a storm
would move into the area			indication that the storm was coming
			Indication of a storm moving into the area
within the next 2 to 3 hours			a phrase meaning about 2 or 3 hours
and remain until morning.			indication that the storm would stay until morning
			Indication of storm duration
The announcer said			indication that someone was reporting about a storm
the storm could bring hail			indication that hail was possible
and up to 4 inches			*4 inches* is required.
of rain			*rain* is required
and cause the temperature to drop			indication that the temperature would drop or decrease
by 15 degrees.			a relative decrease of 15 degrees is required
			Indication of storm's activity
Joe decided to stay home.			indication that he decided to stay home
			Indication that the character decided to stay in
He took off his coat			indication that he took off outer clothing
and sat down			indication that he was sitting down
to watch old films.			indication of viewing films is required
			Indication that the character decided to watch a film or TV

Story B Recall Unit Score Range = 0 to 25 ☐☐ Story B Thematic Unit Score Range = 0 to 8

Recall Total Score Range = 0 to 50 ☐☐ Thematic Total Score Range = 0 to 15

(Sum Recall Unit Scores for Story A & Story B)

(Sum Thematic Unit Scores for Story A & Story B)

12. Logical Memory II *(continued)*

Recognition

RECORDING: Circle Y or N

SCORING RULE: 0-1 pt. for each item

Item	Circle Y or N	Score 0 or 1
Story A		
1. Was the woman's name Anna Thompson?	Y N	
2. Was the story setting in South London?	Y N	
3. Was the woman a cook?	Y N	
4. Did she work in a canteen?	Y N	
5. Did she have four children?	Y N	
6. Were the children teenagers?	Y N	
7. Did the robbery take place on the High Street?	Y N	
8. Did the woman report being robbed two nights before?	Y N	
9. Did she report the robbery at the Police Station?	Y N	
10. Was the woman robbed of 75 pounds?	Y N	
11. Did the family go without food for four days?	Y N	
12. Was the rent due?	Y N	
13. Did the police catch the thief?	Y N	
14. Did the police feel sorry for the woman?	Y N	
15. Did the police make up a collection?	Y N	
Story B		
16. Was the man's name Joe Green?	Y N	
17. Was it Sunday evening?	Y N	
18. Was it 6:00?	Y N	
19. Was the story setting in Liverpool?	Y N	
20. Was Joe dressing to go out?	Y N	
21. Was Joe watching television?	Y N	
22. Was the programme interrupted?	Y N	
23. Was the storm expected to move into the area on Tuesday?	Y N	
24. Was the storm expected to stay in the area through the night?	Y N	
25. Was the temperature predicted to drop 30 degrees?	Y N	
26. Did the announcer predict 10 inches of rain?	Y N	
27. Did the announcer warn of possible flooding?	Y N	
28. Did the announcer warn that it could hail?	Y N	
29. Did Joe decide to stay home?	Y N	
30. Did Joe sit down to watch a sports programme?	Y N	

Recognition Total Score Range = 0 to 30

Percent Retention Calculation

☐ ÷ ☐ x 100 = ☐ Percent Retention Range = 0 to 100%

Logical Memory II Recall Total Score Range = 0 to 50

Logical Memory I Story A Recall Unit Score + Story B-2nd Recall Unit Score Range = 0 to 50

5.8 Wechsler Adult Intelligence Scale -III

WAIS-III Answer Sheet

Time interval: present

Interviewer : .... **Date** |__|__|-|__|__|-|**2**|**0**|__|__|

1. Digital Symbol Coding

Time Limit	120 seconds
Completion Time	
Total Raw Score	(Maximum =133)

2. Arithmetic

	Problem	Time Limit (seconds)	Completion Time in Seconds	Correct Response	Response	Score (0 or 1)
	1	15		3		
	2	15		7		
	3	15		5		
	4	15		2		
Start→	5	15		£9.00		
	7	30		5		
	9	30		8		
	11	30		£10.50		
	13	60		£186.00		
	15	60		£600.00		
	17	60		£51.00		
	19	60		1 of 4 or 5 of 20		0 1 (11-60s) 2 (1-10s)
					Total Raw Score	

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Page 1

3. Block Design

EXAMINEE

	Correct Design	Time Limit	Incorrect Design	Completion Time in Seconds	Correct Design	Score (Circle the appropriate score for each design.)
	1.	30"	Trial 1 Trial 2		Y N	0 Trial 2 1 Trial 1 2
	2.	30"	Trial 1 Trial 2		Y N	0 Trial 2 1 Trial 1 2
	3.	30"	Trial 1 Trial 2		Y N	0 Trial 2 1 Trial 1 2
	4.	30"	Trial 1 Trial 2		Y N	0 Trial 2 1 Trial 1 2
START	5.	60"	Trial 1 Trial 2		Y N	0 Trial 2 1 Trial 1 2
	7.	60"			Y N	0 16"–60" 4 11"–15" 5 6"–10" 6 1"–5" 7
	9.	60"			Y N	0 21"–60" 4 16"–20" 5 11"–15" 6 1"–10" 7
	11.	120"			Y N	0 66"–120" 4 46"–65" 5 31"–45" 6 1"–30" 7
	13.	120"			Y N	0 76"–120" 4 56"–75" 5 41"–55" 6 1"–40" 7

EXAMINER

Total Raw Score

4. Information

	Item	Question	Response	Score (0 or 1)
	1	Saturday		
	2	Age		
	3	Ball		
	4	Months		
Start→	6	Sunrise		
	9	Brazil		
	12	Cleopatra		
	15	Olympics		
	18	Sistine Chapel		
	21	Water		
	24	Continents		
	27	Speed of Light		
			Total Raw Score	

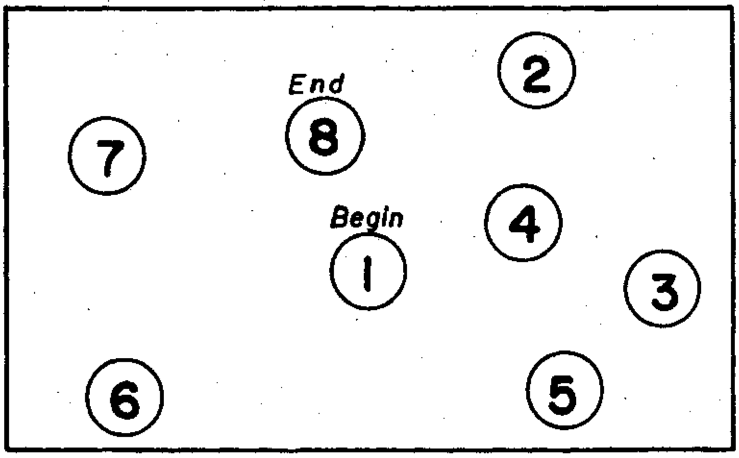
5.9 Trail Making Task

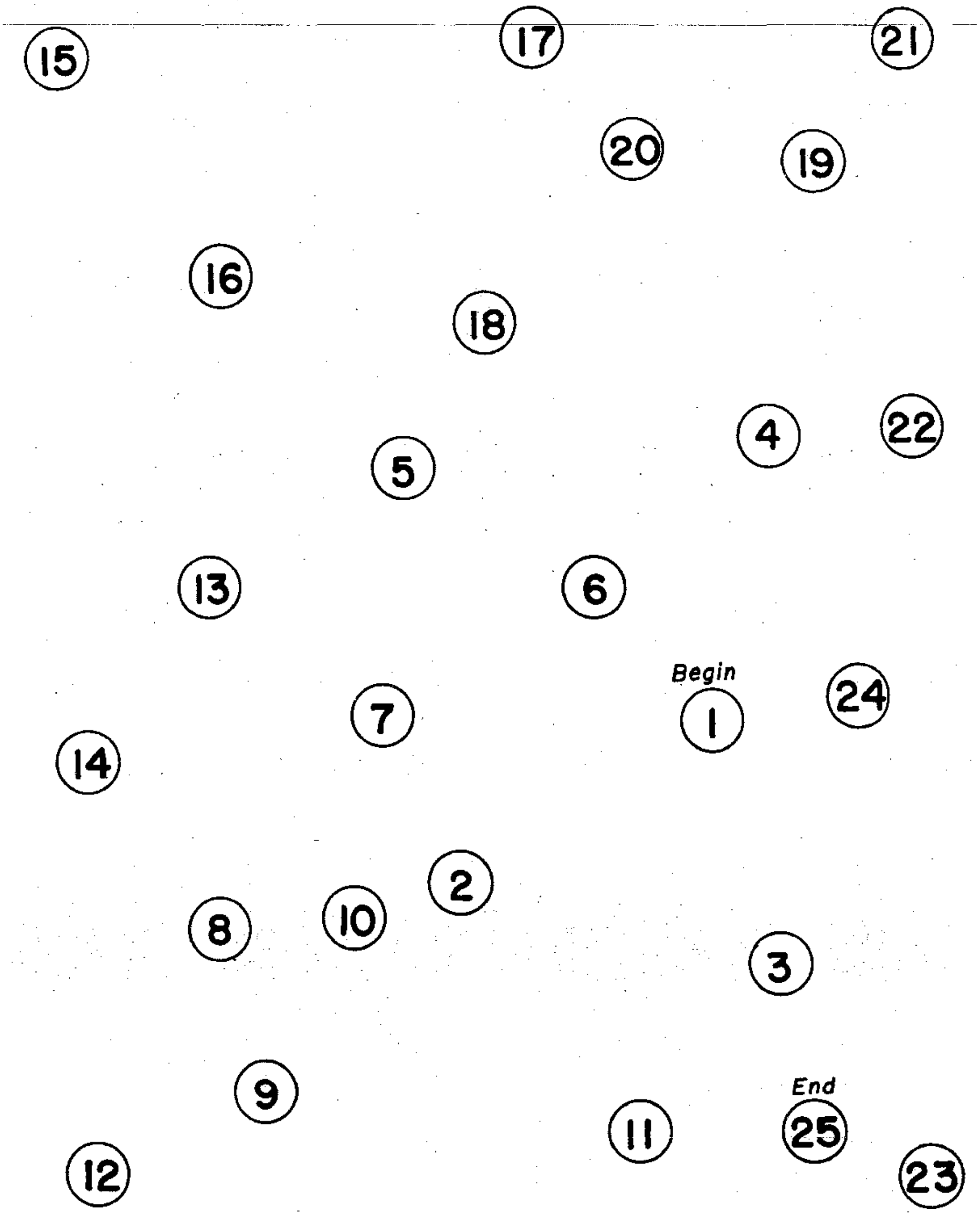
Date of issue: 04/04/2013
Version number: 1

TRAIL MAKING

Part A

SAMPLE

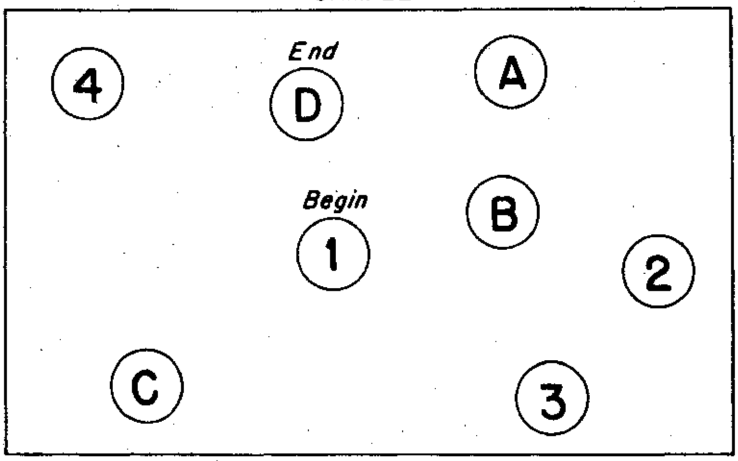


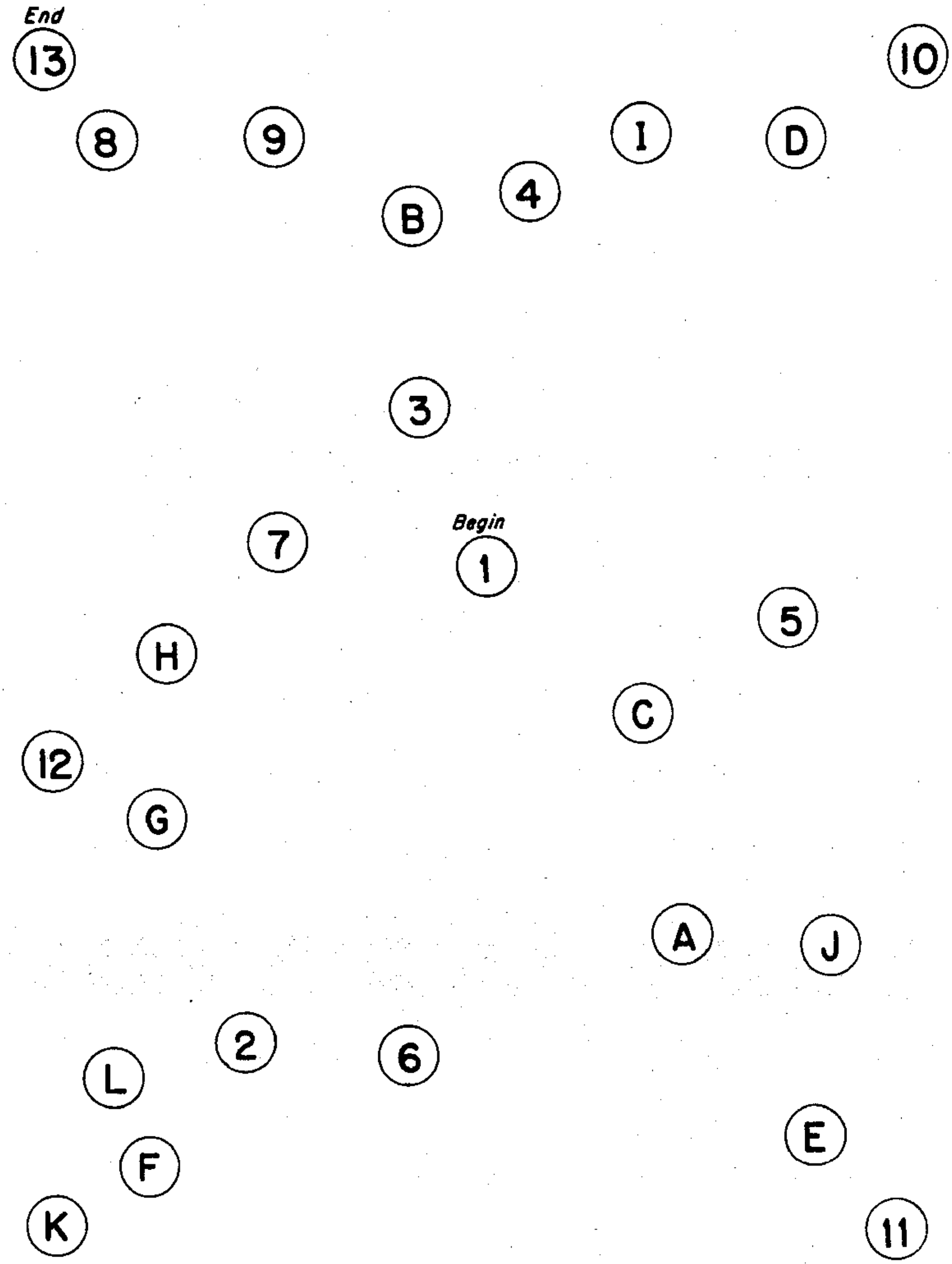

15
17
21
20
19
16
18
4
22
5
13
6
Begin
1
24
7
14
2
8
10
3
9
End
25
11
12
23

TRAIL MAKING

Part B

SAMPLE




End
13
10
8
9
I
D
4
B
3
Begin
1
7
5
H
C
12
G
A
J
2
6
L
E
F
K
11

5.10 Brixton Task

The Brixton Spatial Anticipation Test

- *'There are many pages here which all have the same basic design on them. There are always ten positions, and one of them is always coloured blue'* [point to filled circle on page one]. *'However the coloured one moves around according to various patterns that come and go without warning. These numbers* [point to numbers underneath the circles] *are just here to refer to the position – there is nothing complicated or mathematical about this test'.*
- *'Now, as I turn the pages over, your job is to pick up on the pattern as best you can, and point to where you think the blue one is going to be on the next page. It's not guess-work – you can work it out. For instance, imagine the blue one was here* [point to position 6], *and then when I turn the page it goes to 7, and then to 8, then to 9 – you might reasonably expect it next to go to 10'.*
- *'From time to time the pattern changes without warning, and then it is your job to pick up on the new pattern as best you can. Do you understand?'*
- Give further assistance if necessary
- *'Obviously the first time you have nothing to go on, so your first answer will have to be a guess – have a guess as to where the blue one will be next'*

Item/ page	Correct answer	Subject's response	Correct/ incorrect
1	any		
2	3		☐
3	4		☐
4	5		☐
5	6		☐
6 *	7		☐
7	4		☐
8	3		☐
9	2		☐
10	1		☐
11	10		☐
12 *	9		☐
13	10		☐
14	5		☐
15	10		☐
16	5		☐
17	10		☐
18	5		☐
19 *	10		☐
20	7		☐
21	8		☐
22	9		☐
23	10		☐
24	1		☐
25	2		☐
26 *	3		☐
27	10		☐
28	9		☐

Item/ page	Correct answer	Subject's response	Correct/ incorrect
29 *	8		☐
30	1		☐
31	2		☐
32	3		☐
33	4		☐
34 *	5		☐
35	4		☐
36	10		☐
37	4		☐
38	10		☐
39	4		☐
40	10		☐
41 *	4		☐
42	9		☐
43	9		☐
44	9		☐
45	9		☐
46	9		☐
47	9		☐
48 *	9		☐
49	9		☐
50	8		☐
51	9		☐
52	8		☐
53	9		☐
54	8		☐
55	9		☐

Total number of errors (raw score)

Scaled score

Table D

Raw score	Scaled score	Classification
0–7	10	Very superior
8	9	Superior
9–10	8	Good
11–13	7	High average
14–17	6	Average
18–20	5	Moderate ave.
21–23	4	Low average
24–25	3	Poor
26–31	2	Abnormal
> 31	1	Impaired

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5.10 VERBAL FLUENCY TASK

VERBAL FLUENCY (FAS)

VERBAL FLUENCY

	Total Correct		Total Repeated		Total Errors (Excluding repetitions)	
	60 sec	30 sec	60 sec	30 sec	60 sec	30sec
Letters						
Categories						

11.1 BATCH PROCESSING SCRIPT

The following script was run in SPM-8 to run the pre-processing portion of the structural imaging analysis, as detailed in Chapter 11.1.2.

****

```
matlabbatch{1}.spm.tools.preproc8.channel.vols = {
'/home/k1191125/aPhD/allNIfTI/co20130425_152055BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20130718_161106BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20130801_140532BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20130808_151029BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20131024_142557BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20140109_145918BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20140120_110543BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20140210_111320BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20140213_141135BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20140428_110156BRCAD3s003a1001.nii,1'
'/home/k1191125/aPhD/allNIfTI/co20140508_152233BRCAD3s003a1001A.nii,1'
                                        };
%%
matlabbatch{1}.spm.tools.preproc8.channel.biasreg = 0.0001;
matlabbatch{1}.spm.tools.preproc8.channel.biasfwhm = 60;
matlabbatch{1}.spm.tools.preproc8.channel.write = [0 0];
matlabbatch{1}.spm.tools.preproc8.tissue(1).tpm = {'/cns_zfs/system/system_s9_sparc/spm/spm-8/toolbox/Seg/TPM.nii,1'};
matlabbatch{1}.spm.tools.preproc8.tissue(1).ngaus = 2;
matlabbatch{1}.spm.tools.preproc8.tissue(1).native = [1 1];
matlabbatch{1}.spm.tools.preproc8.tissue(1).warped = [0 0];
matlabbatch{1}.spm.tools.preproc8.tissue(2).tpm = {'/cns_zfs/system/system_s9_sparc/spm/spm-8/toolbox/Seg/TPM.nii,2'};
matlabbatch{1}.spm.tools.preproc8.tissue(2).ngaus = 2;
matlabbatch{1}.spm.tools.preproc8.tissue(2).native = [1 1];
matlabbatch{1}.spm.tools.preproc8.tissue(2).warped = [0 0];
matlabbatch{1}.spm.tools.preproc8.tissue(3).tpm = {'/cns_zfs/system/system_s9_sparc/spm/spm-8/toolbox/Seg/TPM.nii,3'};
matlabbatch{1}.spm.tools.preproc8.tissue(3).ngaus = 2;
matlabbatch{1}.spm.tools.preproc8.tissue(3).native = [1 0];
matlabbatch{1}.spm.tools.preproc8.tissue(3).warped = [0 0];
matlabbatch{1}.spm.tools.preproc8.tissue(4).tpm = {'/cns_zfs/system/system_s9_sparc/spm/spm-8/toolbox/Seg/TPM.nii,4'};
matlabbatch{1}.spm.tools.preproc8.tissue(4).ngaus = 3;
matlabbatch{1}.spm.tools.preproc8.tissue(4).native = [0 0];
```

```
matlabbatch{1}.spm.tools.preproc8.tissue(4).warped = [0 0];
matlabbatch{1}.spm.tools.preproc8.tissue(5).tpm = {'/cns_zfs/system/system_s9_sparc/spm/spm-8/toolbox/Seg/TPM.nii,5'};
matlabbatch{1}.spm.tools.preproc8.tissue(5).ngaus = 4;
matlabbatch{1}.spm.tools.preproc8.tissue(5).native = [0 0];
matlabbatch{1}.spm.tools.preproc8.tissue(5).warped = [0 0];
matlabbatch{1}.spm.tools.preproc8.tissue(6).tpm = {'/cns_zfs/system/system_s9_sparc/spm/spm-8/toolbox/Seg/TPM.nii,6'};
matlabbatch{1}.spm.tools.preproc8.tissue(6).ngaus = 2;
matlabbatch{1}.spm.tools.preproc8.tissue(6).native = [0 0];
matlabbatch{1}.spm.tools.preproc8.tissue(6).warped = [0 0];
matlabbatch{1}.spm.tools.preproc8.warp.mrf = 0;
matlabbatch{1}.spm.tools.preproc8.warp.reg = 4;
matlabbatch{1}.spm.tools.preproc8.warp.affreg = 'mni';
matlabbatch{1}.spm.tools.preproc8.warp.samp = 3;
matlabbatch{1}.spm.tools.preproc8.warp.write = [0 0];
%%
matlabbatch{2}.spm.tools.dartel.warp.images = {
                                {

'/home/k1191125/aPhD/allNIfTI/rc1co20130425_152055BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20130718_161106BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20130801_140532BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20130808_151029BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20131024_142557BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20140109_145918BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20140120_110543BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20140210_111320BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20140213_141135BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20140428_110156BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc1co20140508_152233BRCAD3s003a1001A.nii,1'
                                }
                                {

'/home/k1191125/aPhD/allNIfTI/rc2co20130425_152055BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20130718_161106BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20130801_140532BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20130808_151029BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20131024_142557BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20140109_145918BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20140120_110543BRCAD3s003a1001.nii,1'
```

```
'/home/k1191125/aPhD/allNIfTI/rc2co20140210_111320BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20140213_141135BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20140428_110156BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/rc2co20140508_152233BRCAD3s003a1001A.nii,1'
                                   }
                                   }';
%%
matlabbatch{2}.spm.tools.dartel.warp.settings.template = 'Template';
matlabbatch{2}.spm.tools.dartel.warp.settings.rform = 0;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(1).its = 3;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(1).rparam = [4 2 1e-06];
matlabbatch{2}.spm.tools.dartel.warp.settings.param(1).K = 0;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(1).slam = 16;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(2).its = 3;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(2).rparam = [2 1 1e-06];
matlabbatch{2}.spm.tools.dartel.warp.settings.param(2).K = 0;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(2).slam = 8;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(3).its = 3;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(3).rparam = [1 0.5 1e-06];
matlabbatch{2}.spm.tools.dartel.warp.settings.param(3).K = 1;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(3).slam = 4;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(4).its = 3;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(4).rparam = [0.5 0.25 1e-06];
matlabbatch{2}.spm.tools.dartel.warp.settings.param(4).K = 2;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(4).slam = 2;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(5).its = 3;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(5).rparam = [0.25 0.125 1e-06];
matlabbatch{2}.spm.tools.dartel.warp.settings.param(5).K = 4;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(5).slam = 1;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(6).its = 3;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(6).rparam = [0.25 0.125 1e-06];
matlabbatch{2}.spm.tools.dartel.warp.settings.param(6).K = 6;
matlabbatch{2}.spm.tools.dartel.warp.settings.param(6).slam = 0.5;
matlabbatch{2}.spm.tools.dartel.warp.settings.optim.lmreg = 0.01;
matlabbatch{2}.spm.tools.dartel.warp.settings.optim.cyc = 3;
matlabbatch{2}.spm.tools.dartel.warp.settings.optim.its = 3;
matlabbatch{3}.spm.tools.dartel.mni_norm.template =
{'/home/k1191125/aPhD/allNIfTI/Template_6.nii'};
%%
matlabbatch{3}.spm.tools.dartel.mni_norm.data.subjs.flowfields = {

'/home/k1191125/aPhD/allNIfTI/u_rc1co20130425_152055BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20130718_161106BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20130801_140532BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20130808_151029BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20131024_142557BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20140109_145918BRCAD3s003a1001_Template.nii'
```

```
'/home/k1191125/aPhD/allNIfTI/u_rc1co20140120_110543BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20140210_111320BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20140213_141135BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20140428_110156BRCAD3s003a1001_Template.nii'

'/home/k1191125/aPhD/allNIfTI/u_rc1co20140508_152233BRCAD3s003a1001A_Template.nii'
                                        };
%%
%%
matlabbatch{3}.spm.tools.dartel.mni_norm.data.subjs.images = {
                                      {

'/home/k1191125/aPhD/allNIfTI/c1co20130425_152055BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20130718_161106BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20130801_140532BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20130808_151029BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20131024_142557BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20140109_145918BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20140120_110543BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20140210_111320BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20140213_141135BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20140428_110156BRCAD3s003a1001.nii'

'/home/k1191125/aPhD/allNIfTI/c1co20140508_152233BRCAD3s003a1001A.nii'
                                      }
                                      }';
%%
matlabbatch{3}.spm.tools.dartel.mni_norm.vox = [NaN NaN NaN];
matlabbatch{3}.spm.tools.dartel.mni_norm.bb = [NaN NaN NaN
                              NaN NaN NaN];
matlabbatch{3}.spm.tools.dartel.mni_norm.preserve = 1;
matlabbatch{3}.spm.tools.dartel.mni_norm.fwhm = [10 10 10];
```

****

11.2 TOTAL INTRACRANIAL VOLUME CALCULATION SCRIPT

The following script was run in SPM-8 to calculate the Total Intracranial Volume (TIV) of each individual MR scan, as detailed in Chapter 11.1.3. 'Image' denotes the scans of interest, in this case the scans of our 11 (metacognitive study) or 15 (BCIS study) patients. This code was run three times to calculate the volume of segmented gray matter, white matter and CSF files. The totals were then summed to produce individual TIVs.

```
************************
V = spm_vol(spm_select(Inf,'Image'));
Vols = zeros(numel(V),1);
for j=1:numel(V),
  tot = 0;
  for i=1:V(1).dim(3),
      img = spm_slice_vol(V(j),spm_matrix(...
          [0 0 i]),V(j).dim(1:2),0);
      img = img(isfinite(img)); % <-- exclude non-finite values
      tot = tot + sum(img(:));
  end;
  voxvol = abs(det(V(j).mat))/100^3; % volume of a voxel, in litres
  Vols(j) = tot*voxvol;
end
************************
```

11.3 STATISTICAL ANALYSIS

The following script was run in SPM-8 to carry out the multiple regression analysis, designed to investigate the relationship between brain structure and memory metacognitive efficiency.

****

```
matlabbatch{1}.spm.stats.factorial_design.dir = {'/home/k1191125/aPhD/Results/'};
%%
matlabbatch{1}.spm.stats.factorial_design.des.mreg.scans = {

'/home/k1191125/aPhD/allNIfTI/smwc1co20130425_152055BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20130718_161106BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20130801_140532BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20130808_151029BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20131024_142557BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20140109_145918BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20140120_110543BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20140210_111320BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20140213_141135BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20140428_110156BRCAD3s003a1001.nii,1'

'/home/k1191125/aPhD/allNIfTI/smwc1co20140508_152233BRCAD3s003a1001A.nii,1'
                                      };
%%
%%
matlabbatch{1}.spm.stats.factorial_design.des.mreg.mcov(1).c = [-0.428847056
                                        -0.473994666
                                        0.882228955
                                        0.385183338
                                        0.84786824
                                        2.026132448
                                        -0.21836638
                                        1.030925043
                                        1.008204452
                                        0.568156738
                                        1.086397632];
%%
matlabbatch{1}.spm.stats.factorial_design.des.mreg.mcov(1).cname = 'MetaD';
matlabbatch{1}.spm.stats.factorial_design.des.mreg.mcov(1).iCC = 5;
%%
matlabbatch{1}.spm.stats.factorial_design.des.mreg.mcov(2).c = [83
                                        78
```

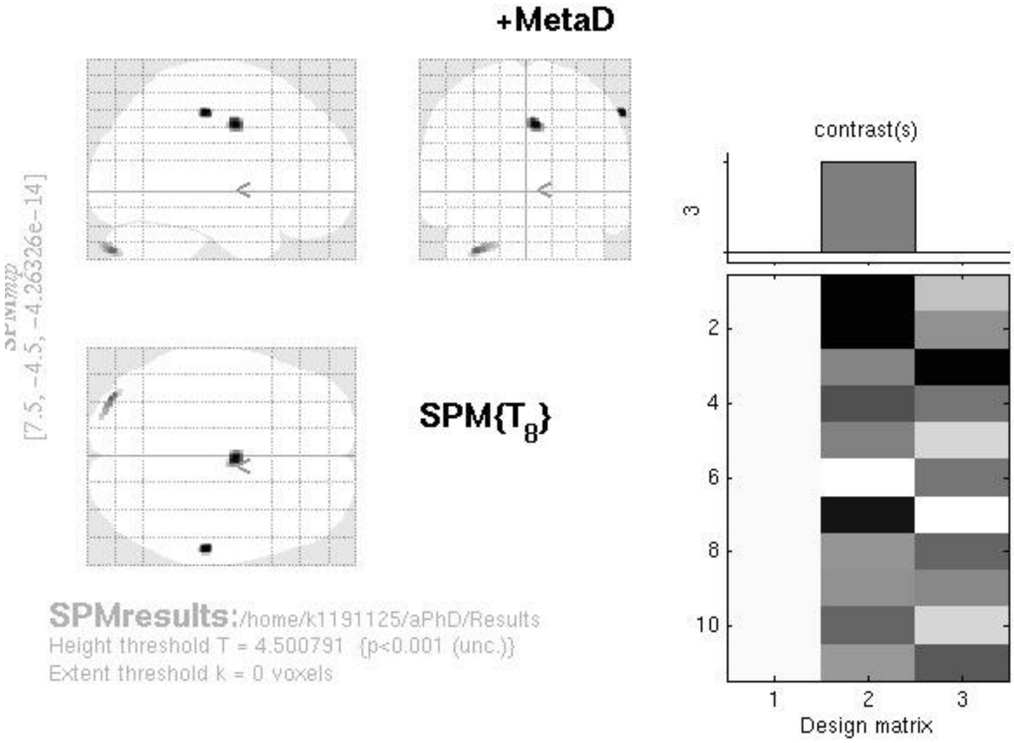
```
                                        62
                                        75
                                        85
                                        75
                                        89
                                        73
                                        77
                                        85
                                        72];
%%
matlabbatch{1}.spm.stats.factorial_design.des.mreg.mcov(2).cname = 'Age';
matlabbatch{1}.spm.stats.factorial_design.des.mreg.mcov(2).iCC = 5;
matlabbatch{1}.spm.stats.factorial_design.des.mreg.incint = 1;
matlabbatch{1}.spm.stats.factorial_design.cov = struct('c', {}, 'cname', {}, 'iCFI', {}, 'iCC', {});
matlabbatch{1}.spm.stats.factorial_design.masking.tm.tma.athresh = 0.2;
matlabbatch{1}.spm.stats.factorial_design.masking.im = 1;
matlabbatch{1}.spm.stats.factorial_design.masking.em = {''};
%%
matlabbatch{1}.spm.stats.factorial_design.globalc.g_user.global_uval = [1.55684867185684
                                        1.67147945387115
                                        1.27387874635969
                                        1.63284839766178
                                        1.64284727043351
                                        1.36569485700055
                                        1.6436866321893
                                        1.64311831687576
                                        1.61066193131368
                                        1.36548152885445
                                        1.53515697807603];
%%
matlabbatch{1}.spm.stats.factorial_design.globalm.gmsca.gmsca_no = 1;
matlabbatch{1}.spm.stats.factorial_design.globalm.glonorm = 2;
matlabbatch{2}.spm.stats.fmri_est.spmmat(1) = cfg_dep;
matlabbatch{2}.spm.stats.fmri_est.spmmat(1).tname = 'Select SPM.mat';
matlabbatch{2}.spm.stats.fmri_est.spmmat(1).tgt_spec{1}(1).name = 'filter';
matlabbatch{2}.spm.stats.fmri_est.spmmat(1).tgt_spec{1}(1).value = 'mat';
matlabbatch{2}.spm.stats.fmri_est.spmmat(1).tgt_spec{1}(2).name = 'strtype';
matlabbatch{2}.spm.stats.fmri_est.spmmat(1).tgt_spec{1}(2).value = 'e';
matlabbatch{2}.spm.stats.fmri_est.spmmat(1).sname = 'Factorial design specification: SPM.mat File';
matlabbatch{2}.spm.stats.fmri_est.spmmat(1).src_exbranch = substruct('.','val', '{}',{1}, '.','val', '{}',{1},
'.','val', '{}',{1});
matlabbatch{2}.spm.stats.fmri_est.spmmat(1).src_output = substruct('.','spmmat');
matlabbatch{2}.spm.stats.fmri_est.method.Classical = 1;
matlabbatch{3}.spm.stats.con.spmmat(1) = cfg_dep;
matlabbatch{3}.spm.stats.con.spmmat(1).tname = 'Select SPM.mat';
matlabbatch{3}.spm.stats.con.spmmat(1).tgt_spec{1}(1).name = 'filter';
matlabbatch{3}.spm.stats.con.spmmat(1).tgt_spec{1}(1).value = 'mat';
matlabbatch{3}.spm.stats.con.spmmat(1).tgt_spec{1}(2).name = 'strtype';
matlabbatch{3}.spm.stats.con.spmmat(1).tgt_spec{1}(2).value = 'e';
matlabbatch{3}.spm.stats.con.spmmat(1).sname = 'Model estimation: SPM.mat File';
matlabbatch{3}.spm.stats.con.spmmat(1).src_exbranch = substruct('.','val', '{}',{2}, '.','val', '{}',{1},
'.','val', '{}',{1});
matlabbatch{3}.spm.stats.con.spmmat(1).src_output = substruct('.','spmmat');
matlabbatch{3}.spm.stats.con.consess{1}.tcon.name = '+MetaD';
matlabbatch{3}.spm.stats.con.consess{1}.tcon.convec = 1;
matlabbatch{3}.spm.stats.con.consess{1}.tcon.sessrep = 'none';
matlabbatch{3}.spm.stats.con.consess{2}.tcon.name = '-MetaD';
```

```
matlabbatch{3}.spm.stats.con.consess{2}.tcon.convec = -1;
matlabbatch{3}.spm.stats.con.consess{2}.tcon.sessrep = 'none';
matlabbatch{3}.spm.stats.con.delete = 0;
```

11.4 Raw SPM output

11.4.1 Metacognitive efficiency

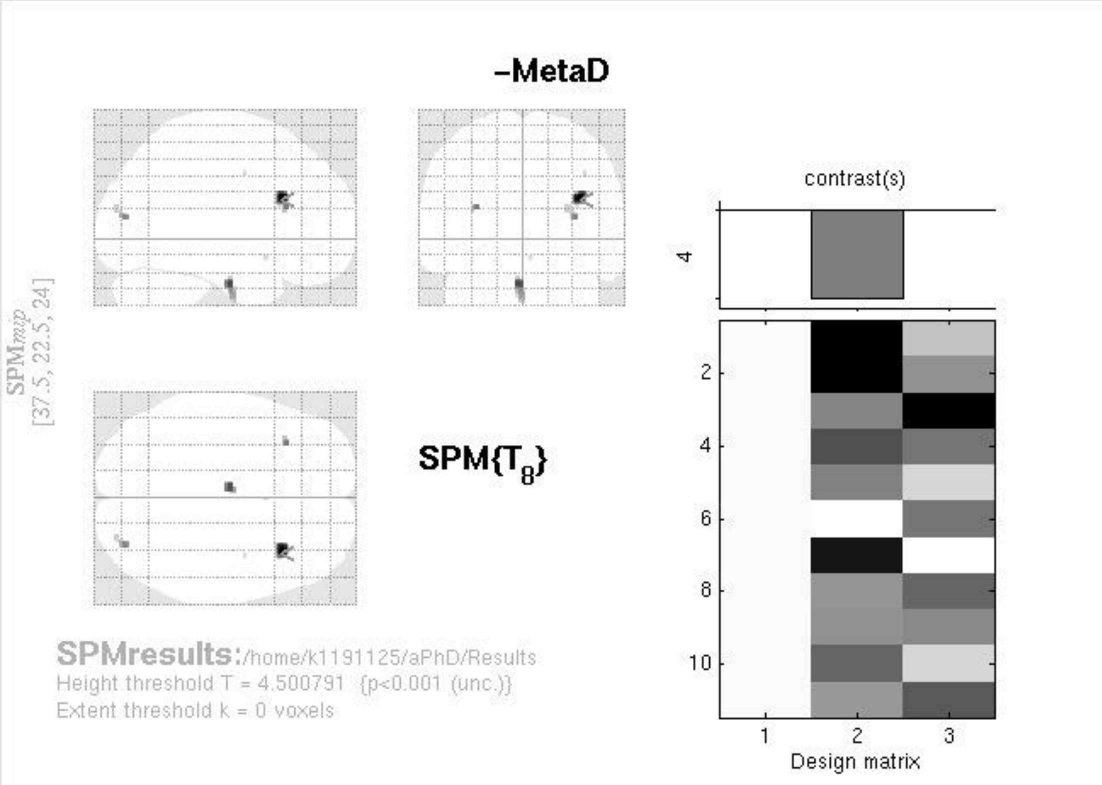
Figure A.11.4-1 is the raw SPM output displaying the “glass brain view” of the positive associations between gray matter volume and metacognitive efficiency. Figure A.11.4-2 is the raw SPM output displaying the “glass brain view” of the negative associations between gray matter volume and metacognitive efficiency. Gray and black ‘blobs’ indicate significant areas of gray matter associated with metacognitive efficiency in the axial, sagittal and coronal views. The reported statistics demonstrate the corrected and uncorrected significance values for clusters and peak voxels of gray matter associated with metacognitive efficiency.



Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm	mm	mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_\equiv)$	p_{uncorr}			
1.000	3	0.943	0.463	96	0.215	0.983	0.752	6.31	3.68	0.000	3	-7	40
		0.998	0.463	34	0.463	0.985	0.752	6.26	3.67	0.000	60	-27	48
		0.995	0.463	45	0.396	0.999	0.752	5.46	3.43	0.000	-33	-87	-39

Figure A.11.4-1 Glass brain view, cluster statistics and peak voxel statistics for metacognitive efficiency statistical analysis (positive).



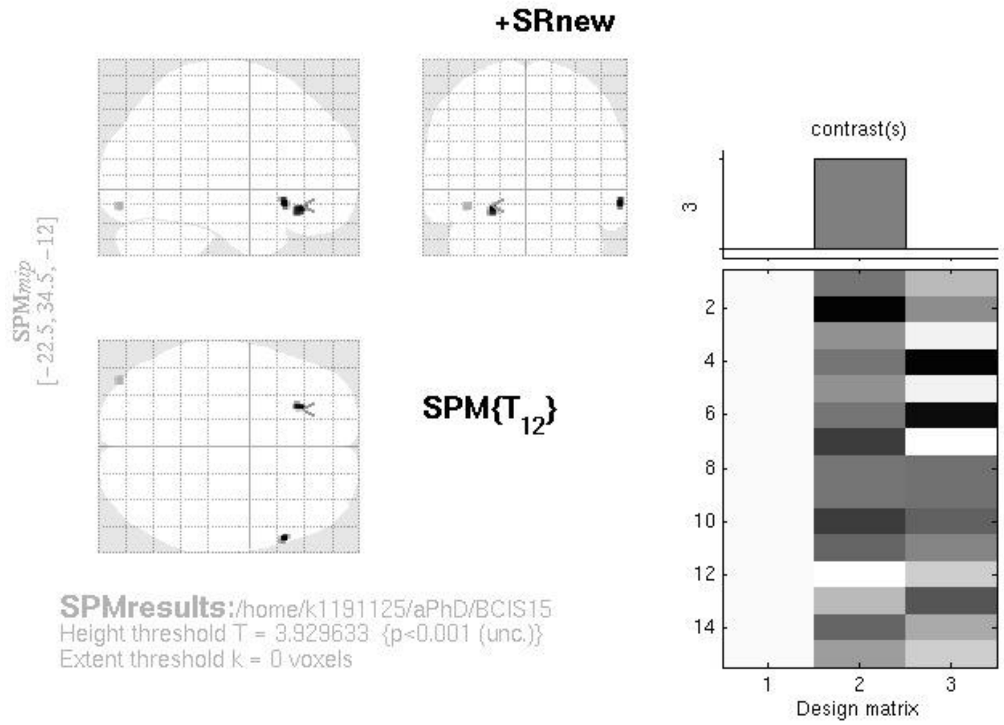
Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_{\equiv})$	p_{uncorr}	
0.991	6	0.988	0.929	58	0.333	0.999	0.980	5.40	3.41	0.000	-4 -13 -30
		1.000	0.929	17	0.616	1.000	0.980	5.04	3.29	0.000	33 -82 12

Figure A.11.4-2 Glass brain view, cluster statistics and peak voxel statistics for metacognitive efficiency statistical analysis (negative).

11.4.2 BCIS SELF-REFLECTION

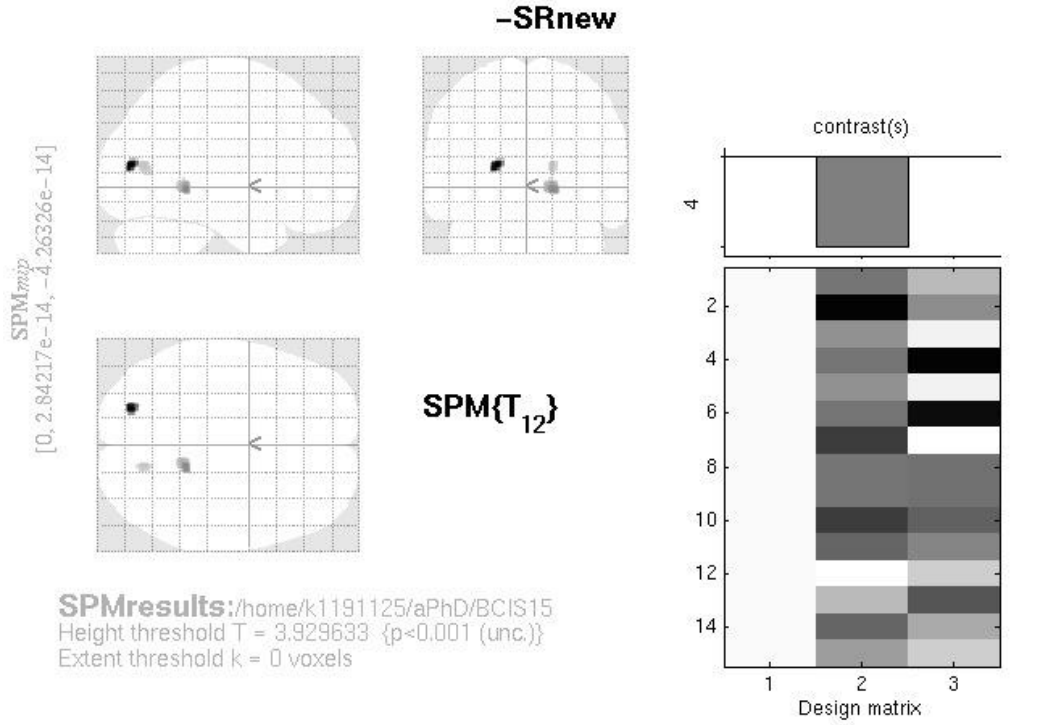
Figure A.11.4-3 is the raw SPM output displaying the “glass brain view” of the positive associations between gray matter volume and BCIS self-reflection (SR). Figure A.11.4-4 is the raw SPM output displaying the “glass brain view” of the negative associations between gray matter volume and metacognitive efficiency. Gray and black ‘blobs’ indicate significant areas of gray matter associated with metacognitive efficiency in the axial, sagittal and coronal views. The reported statistics demonstrate the corrected and uncorrected significance values for clusters and peak voxels of gray matter associated with metacognitive efficiency.



Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_\equiv)$	p_{uncorr}	
0.997	3	0.998	0.665	21	0.637	0.973	0.561	4.84	3.54	0.000	60 20 -11
		0.991	0.665	44	0.477	0.975	0.561	4.82	3.53	0.000	-22 32 -15
		0.999	0.665	18	0.665	1.000	0.806	4.13	3.19	0.001	-40 -88 -14

Figure A.11.4-3 Glass brain view, cluster statistics and peak voxel statistics for SR statistical analysis (positive).



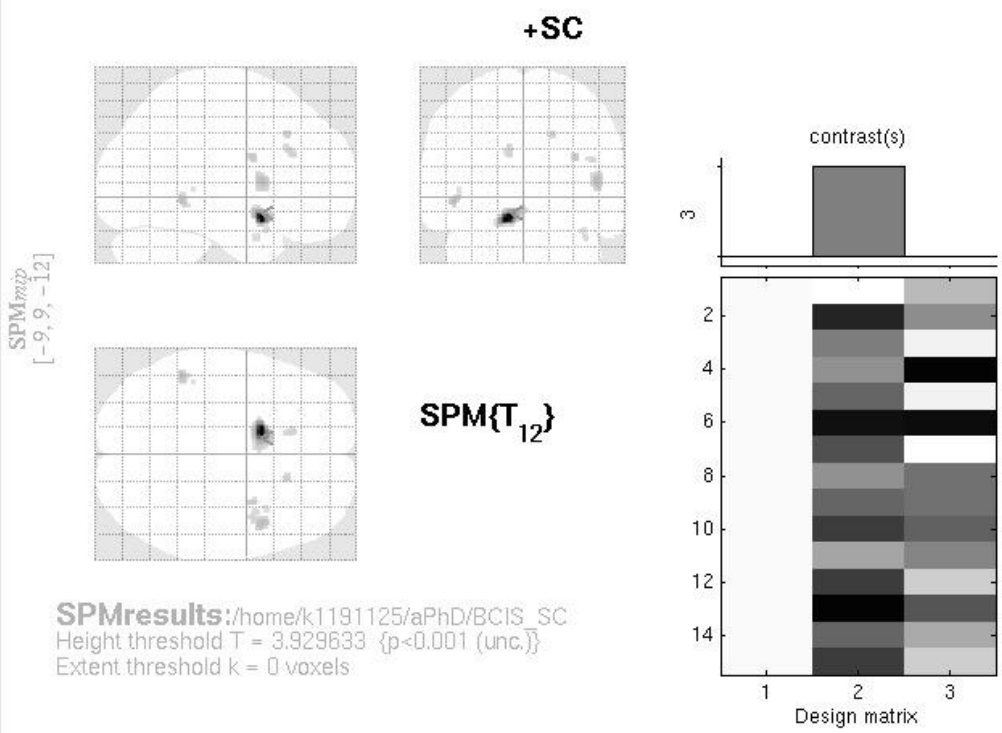
Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_\equiv)$	p_{uncorr}	
0.997	3	0.985	0.557	55	0.424	0.631	0.304	6.03	4.01	0.000	-21 -79 12
		0.929	0.557	104	0.269	0.985	0.639	4.70	3.48	0.000	15 -43 -3
		0.996	0.557	31	0.557	0.999	0.756	4.19	3.22	0.001	15 -72 12

Figure A.11.4-4 Glass brain view, cluster statistics and peak voxel statistics for SR statistical analysis (negative).

11.4.3 BCIS SELF-CERTAINTY

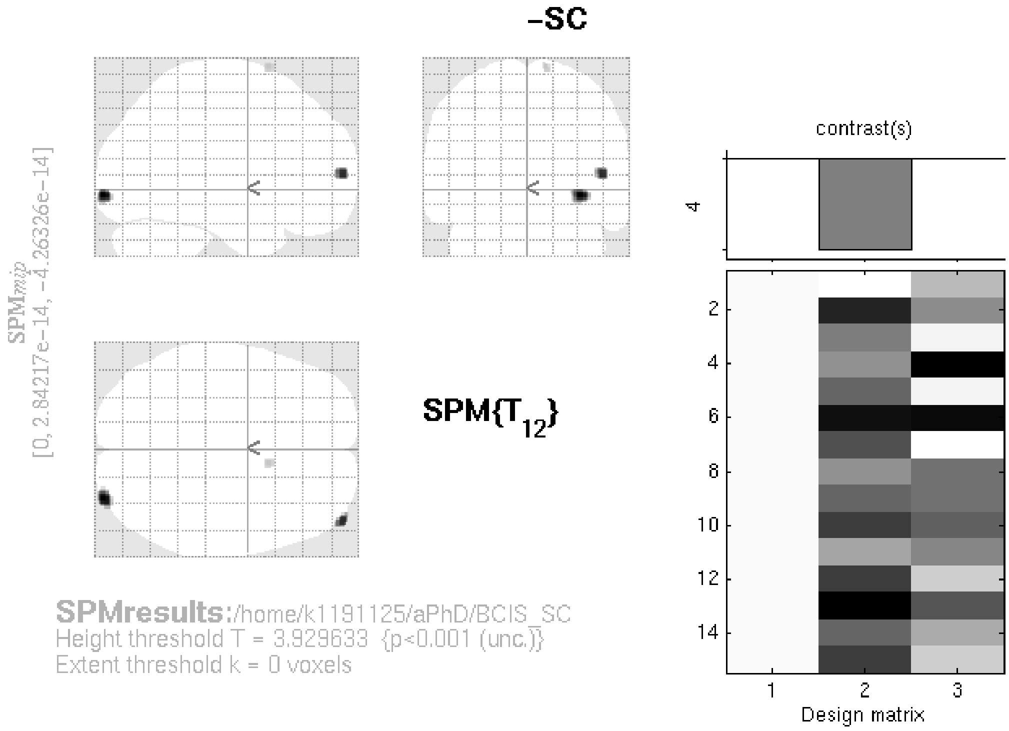
Figure A.11.4-5 is the raw SPM output displaying the “glass brain view” of the positive associations between gray matter volume and BCIS self-certainty (SC). Figure A.11.4-6 is the raw SPM output displaying the “glass brain view” of the negative associations between gray matter volume and SC scores. Gray and black ‘blobs’ indicate significant areas of gray matter associated with SC scores in the axial, sagittal and coronal views. The reported statistics demonstrate the corrected and uncorrected significance values for clusters and peak voxels of gray matter associated with SC scores.



Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm		
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_{\equiv})$	p_{uncorr}			
0.512	10	0.513	0.737	294	0.074	0.008	0.008	11.53	5.38	0.000	-12	8	-15
		0.992	0.943	41	0.496	0.901	0.937	5.24	3.71	0.000	-48	-45	-5
		0.887	0.943	128	0.224	0.936	0.937	5.08	3.64	0.000	46	8	7
		0.999	0.943	11	0.747	0.993	0.963	4.54	3.40	0.000	16	24	37
		0.996	0.943	29	0.573	0.997	0.963	4.38	3.32	0.000	-12	27	25

Figure A.11.4-5 Glass brain view, cluster statistics and peak voxel statistics for SC statistical analysis (positive).



Statistics: ***p-values adjusted for search volume***

set-level		cluster-level				peak-level					mm mm mm
p	c	$p_{FWE-corr}$	$q_{FDR-corr}$	k_E	p_{uncorr}	$p_{FWE-corr}$	$q_{FDR-corr}$	T	$(Z_\equiv)$	p_{uncorr}	
0.997	3	0.900	0.653	121	0.236	0.928	0.543	5.12	3.66	0.000	33 -96 -6
		0.986	0.653	53	0.435	0.971	0.543	4.85	3.54	0.000	46 60 7

Figure A.11.4-6 Glass brain view, cluster statistics and peak voxel statistics for SC statistical analysis (negative).